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THE USE OF ACTH AND CORTISONE IN DISEASE OF CHILDHOOD.[1]

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THIS paper is not a record of personal use of these drugs in the treatment of patients under my care. It is largely gained from a study of the recent literature from abroad and from personal observations made in the United States of America and in Great Britain during 1951. Owing to their scarcity and high price, the use of these drugs in the Royal Alexandra Hospital for Children has been sporadic, and apart from the Institute of Child Health no coordinated plan of study has been made of their effects. Therefore, it is thought that such a paper as this may be of use to those whose personal experience is similarly limited.

There is a certain amount of confusion with regard to the method of administration and to dosage. Corticotrophin or ACTH is given intramuscularly and the total daily dosage is divided into four equal parts given six-hourly. Cortisone has a much more prolonged action, and if given by injection it takes longer to act and may exert its effect for as long as four days. Therefore it is given not more frequently than every twenty-four hours. However, if it is given by mouth its action is very much quicker and of shorter duration. Thus a dosage equal to, or slightly greater than, that given intramuscularly every twenty-four hours should be divided into four and given every six hours by mouth. There may be advantages in giving either preparation intravenously when a quick result or a more massive effect is desired, but with corticotrophin one is using a far from pure biological preparation and anaphylactic reactions may be dangerous.

In Table I, I have suggested minimal effective dosage which can be used as a start. Whether such dosage needs to be increased is a matter of noting the clinical response until further experience indicates the necessity for larger initial amounts. The reduction or maintenance of the circulating eosinophile cells at zero level has been said to indicate sufficient dosage, but recent work seems to indicate that, with corticotrophin at least, the response of the adrenal cortex is such that reduction to this level is attained with a dosage which may not be effective for the condition under treatment (Rapoport, 1951).

Side effects are frequent and sometimes extremely dangerous. The changes similar to Cushing's syndrome, such as "moon" facies, acne, cutaneous striæ and obesity, are reversible and not of importance unless dosage sufficient to bring them about has to be continued for a considerable period. Sodium and water retention with circulatory embarrassment may occur quite suddenly and should be dealt with by mercurial diuretics or temporary

[1] Read at a meeting of the Section of Pædiatrics of the New South Wales Branch of the British Medical Association on July 29, 1952.

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cessation of therapy in some cases. It can be prevented in part by sodium restriction in the diet and should be watched for by noting any sudden increase in the daily recording of the weight and decrease in the urinary output. Loss of body potassium with resultant anorexia, muscle weakness, profound lethargy and changes in the electrocardiogram can be prevented by giving potassium chloride in doses of 2·5 grammes daily. Latent infections can be activated or fresh infections occur very easily, often without any evidence of their presence, such as pyrexia. The routine use of such antibiotics as aureomycin, chloramphenicol or terramycin during the administration of ACTH or cortisone has been advocated in an endeavour to prevent such infections. Hypertension with tachycardia is an effect which should be watched for daily and necessitates suspension of the therapy in most cases. Other complications are likely to occur, as will be mentioned by Dr. Vines in his paper. Possibly further changes will be reported in other studies in the future.

TABLE I.

Suggested Initial Dosage by Intramuscular Injection.

Age. (Years.)	Corticotrophin. Daily Dosage in Four Doses Given Every Six Hours.	Cortisone. Daily Dosage, One Dose Given Every Twenty-four Hours.
0 to 1	10 milligrammes (each dose 2·5 milligrammes).	20 milligrammes.
1 to 5	20 milligrammes (each dose 5·0 milligrammes).	40 milligrammes.
5 to 10	40 milligrammes (each dose 10 milligrammes).	60 milligrammes.
10 to 15	60 to 100 milligrammes (each dose 15 to 25 milligrammes).	100 to 200 milligrammes.

In Figure I, I have illustrated a method by which the adequacy of therapy can be judged and complications detected early. It shows the use of corticotrophin in a patient, aged eleven years, suffering from rheumatic fever.

For the remainder of this paper I shall confine my remarks to the use of these preparations in rheumatic fever, acute leuchæmia, the nephrotic syndrome and juvenile rheumatoid arthritis. In the next paper a further number of diseases responsive to these hormones will be discussed.

Rheumatic Fever.

There is as yet no general agreement as to the efficacy of corticotrophin and cortisone in preventing cardiac damage in rheumatic fever. Barnes (1951) believes that these drugs suppress the acute exudative manifestations until the as yet unknown underlying cause of the exudative phase ceases to act. There is general agreement that the underlying cause is unaffected and that the length of time during which it acts is not shortened. Whether their use will prevent or minimize heart damage will be known only by a long-term study of a large number of patients.

At the present time the American Heart Association and the Medical Research Council of Great Britain have organized a cooperative study involving a number of clinics in North America and Great Britain. All have agreed on certain criteria and standards to be followed in the selection and treatment of patients. Data are kept in a standard way for analysis in a coordinating centre. When this study is finished it is hoped that the position may be much clearer.

We in this country are under a disadvantage, in that supplies of these drugs are small and the price is very high. At present the respective costs of five grammes of cortisone or three grammes of corticotrophin, amounts suitable for treatment of the average patient with rheumatic fever, are £48 and £58 respectively. Therefore it would seem that for the present it is undesirable to treat rheumatic fever with these preparations unless there is clear evidence of carditis. By clear evidence are meant such manifestations as cardiac enlargement, a loud, high-pitched, widely propagated systolic murmur of the "seagull" variety, soft blowing diastolic murmurs at the apex and/or along the left border of the sternum of recent onset, a pericardial friction rub or evidence of cardiac failure. Such signs may be found in patients whose disease is of recent onset or in those patients who have had continuous rheumatic activity with periodic exacerbations for a period of months or even years. At present it would seem that, if carditis is undoubtedly present, corticotrophin or cortisone, given in sufficient dosage for an adequate length of time, offers the best hope of minimizing cardiac damage.

In order to learn as much as possible about the use of these hormones and also to detect the earliest signs of possibly dangerous side reactions, each patient should be carefully studied.

For clinical control frequent complicated laboratory methods do not appear to be necessary beyond a bare minimum. Nearly all the necessary information can be gained by clinical examination by the medical attendant. The usual examinations necessary during administration of these preparations, such as four-hourly recordings of pulse rate, respiration rate, temperature, daily weight, urinary output, blood pressure and number of circulating eosinophile cells, should be carried out. In the estimation of improvement in the clinical condition of the patient careful daily clinical examination is most important. Variation in the position of the apex should be noted and disappearance or variation of intensity or propagation of heart murmurs recorded. Signs of cardiac failure should be looked for, such as engorgement of neck veins, sacral œdema, enlargement of the liver and crepitations at the lung bases. Wilson (1951) has advocated daily estimations of the vital capacity as a means of estimating progress. Serial electrocardiographic records are not necessary, but are of help, in that they show shortening of the auriculoventricular conduction time, if this has been prolonged, and also the earliest evidence of potassium deficiency. Frequent estimations of the erythrocyte sedimentation rate are probably not necessary, as they invariably show a steady fall, which is probably a non-specific effect of treatment. Similarly, hæmoglobin estimations will show a dramatic rise if there has been a previously low level. Radiological examinations of the heart shadow, full blood counts, microscopic examinations of the urine and estimations of the blood electrolyte contents are of great interest, but not essential to the control of therapy.

The dosage used in various reported series has varied. Barnes (1951) gave daily amounts by intramuscular injection of 200 to 300 milligrammes of cortisone or 60 to 100 milligrammes of corticotrophin. These were continued until the acute manifestations were controlled and then reduced substantially for a further period of four to six weeks. Dorfman (1951) used corticotrophin in doses of 80 milligrammes daily for two days; this dosage was then reduced to 40 milligrammes, which was gradually reduced over a further four to six weeks. Wilson (1951) administered 30 to 60 milligrammes of corticotrophin daily for only seven days, but her patients were treated very early in the disease and the evidence of carditis was inconclusive. As there does not seem to be any superiority in the effect of cortisone over corticotrophin, and as the latter is far more readily available, it is suggested that corticotrophin be given at present. The total daily dosage should be 80 milligrammes per day given intramuscularly, divided into four equal doses given every six hours. This dose should be increased or diminished according to the eosinophile cell count and clinical signs, and continued for six weeks.

The clinical response to therapy is now fairly well known. Polyarthritis and fever almost invariably disappear within a week and usually in several days. It should be remembered that salicylates have the same effect. Tachycardia takes longer to be relieved, and in severe cases of long standing may remain unaltered. Nodules disappear in a few weeks. Congestive cardiac failure is nearly always rapidly relieved unless salt and water retention occurs. Cardiac enlargement usually decreases, but may remain the same. The "seagull" murmur eventually disappears, but may become louder first. Other systolic murmurs may become less loud or be unaffected. Diastolic murmurs may

be heard first during the course of therapy, but eventually disappear. Of course, murmurs due to previous attacks remain unchanged. Signs of pericardial friction are heard for a few days only in most cases, but may persist for a few weeks. Bradycardia is not uncommon and does not seem to be of importance. It is interesting that this is also found occasionally with salicylate therapy. Prolongation of the auriculo-ventricular conduction time usually disappears in three weeks.

After therapy has been stopped reappearance of acute signs is very common, and this may occur in from one to seventeen days. This reactivation consists of fever, tachycardia, rise in the erythrocyte sedimentation rate, an increase in the number of circulating eosinophile cells, lengthening of the auriculo-ventricular conduction time, and occasionally polyarthritis. According to Barnes (1951), treatment, if continued long enough, will prevent this, and further treatment for two weeks is indicated if it should

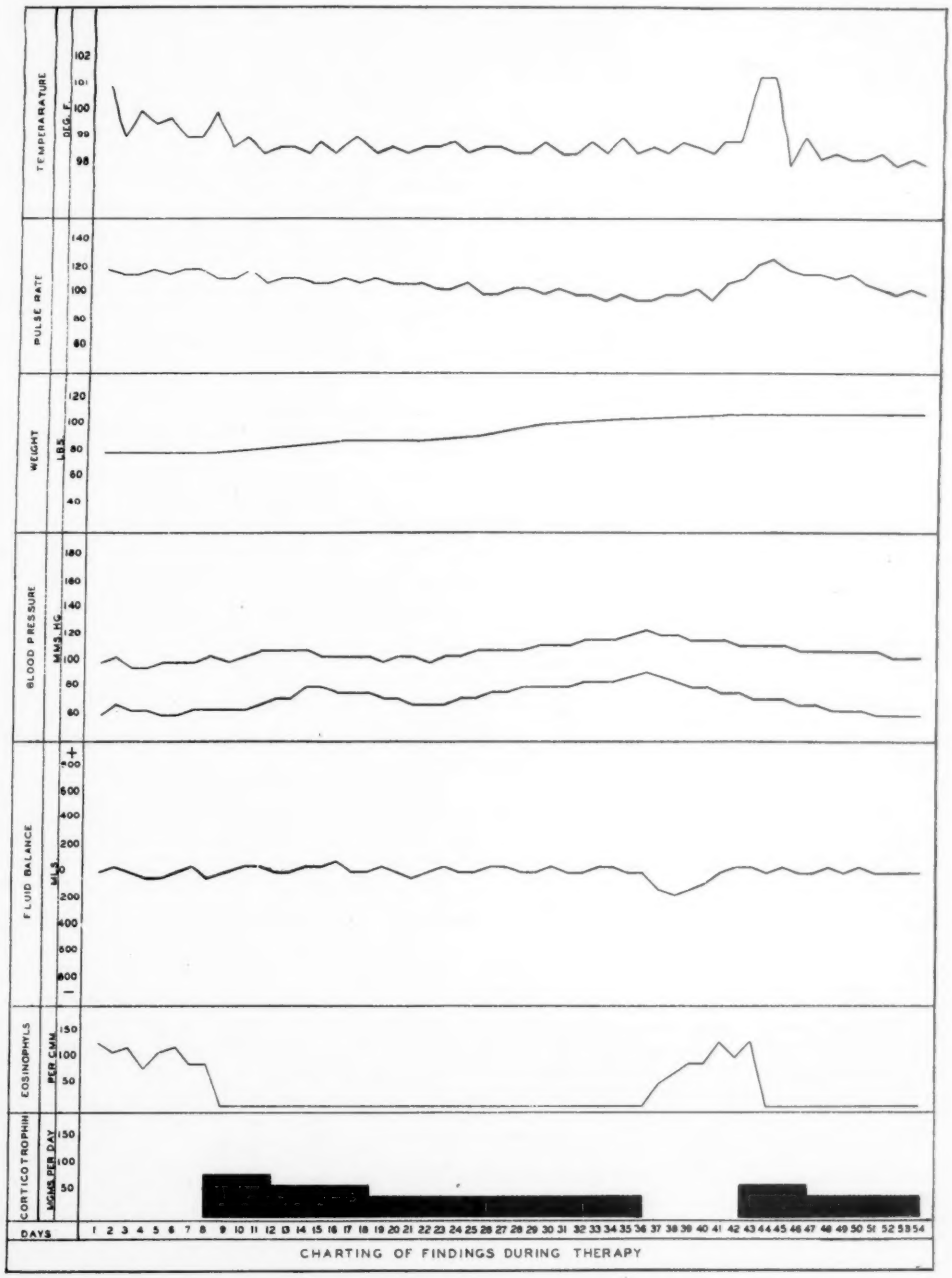

FIGURE I.

occur. Others state that it almost always subsides spontaneously after a few days and rarely causes any anxiety. This reactivation is illustrated in Figure I.

Acute Leuchæmia.

It is now well established that in some of the acute leuchæmias hæmatological remission can be induced and clinical remission obtained for as long as nine months after the administration of corticotrophin or cortisone. Whether the total duration of life is increased by such therapy is not yet clear, but the remissions brought about are accompanied by subjective sensations of well-being not seen in the untreated leuchæmias. There is also good evidence that if a remission cannot be obtained by hormone therapy, the folic acid antagonists may still be effective and *vice versa*. While the folic acid antagonists may produce similar results, toxic side reactions are common and unpleasant.

Hormone treatment is most successful in the acute stem cell leuchæmias, there being little response when the abnormal cells have differentiated beyond the blast stage. Duration of the disease prior to treatment does not appear to affect the response, nor does the prior use of the folic acid antagonists. Schulman (1951) believes that the most successful results can be expected in those patients who have the fewest symptoms and the least evidence of organ enlargement and hæmorrhagic diathesis.

Dosage is purely empirical, as no reliance can be placed on the eosinophile cell response, because these cells are often absent from the peripheral blood at the beginning of therapy. Snelling (1951) used corticotrophin in doses of 80 to 120 milligrammes per day, decreasing to 40 to 60 milligrammes per day in the later stages. He found that in successful cases it required seventeen to thirty-three days for a remission to occur. Schulman (1951) gave slightly smaller doses, namely, 60 milligrammes daily for three days, followed by 40 milligrammes daily until remission occurred. He administered cortisone in doses of 100 to 200 milligrammes daily. Treatment of relapse is along the same lines, but it is generally agreed that remissions so induced are less complete and do not last so long.

Examinations of the blood should be carried out twice a week with estimations of the hæmoglobin value and counting of the erythrocytes, leucocytes, platelets and reticulocytes, including a differential count. Marrow should be obtained by occasional puncture and examined. There is usually a reduction of the blast cells in the peripheral blood at the end of the first week, followed by their slower replacement by neutrophile cells. If there is no initial leucocytosis, the differential count usually becomes normal in three to four weeks. A sudden rise in thrombocytes usually occurs in four to eighteen days. The level of erythrocytes and hæmoglobin may fall in the first few weeks of therapy, but a reticulocyte response is usually evident in the second or third week and transfusions are rarely necessary. In the serial marrow examinations the erythroblastic elements are the first to increase, and maximal marrow improvement is found in three to four weeks.

The weight steadily increases owing to the greatly increased appetite. This does not indicate a remission, being a non-specific effect of therapy. There is striking reduction in the size of the lymph glands, spleen and liver, if enlarged, and in bone pain and manifestations of the bleeding tendency if these are present.

Nobody believes that administration of these hormones can cure leuchæmia, but there is no doubt that they are a great advance in its treatment. The mode of their action in remissions is quite unknown. It is probably not a direct destructive effect on the abnormal cells, as probably occurs with the folic acid antagonists and urethane. Abnormal cells are destroyed and do not mature into mature varieties, but this seems to be due to a restoration of their environment to normal, so that it becomes inimical to them. There also seems to be a stimulation of the marrow in some way so that normal cells are produced.

The Nephrotic Syndrome.

By the nephrotic syndrome is meant that condition which is characterized by generalized œdema, heavy proteinæmia, a low serum protein level and a high blood cholesterol level.

If corticotrophin is administered, significant diuresis will occur in a large proportion of cases, resulting in complete or partial loss of œdema. The dosage used has varied from 40 to 150 milligrammes daily, but it seems that a dose of 50 milligrammes per day is adequate for any child and is as effective in producing diuresis as higher doses. This dosage has been used for periods lasting from four to eighteen days, but ten days is the average. Diuresis can begin as early as the fourth day of therapy, but may not commence till four days after the administration has stopped, and usually continues for about a week.

There is at present no way of knowing which patients will have a successful diuresis. but it seems that success is most likely in those younger children who have the shortest history of illness. The presence or absence of evidence of renal damage has no bearing on the bringing about of a remission.

Serum protein and cholesterol levels show a tendency to return to normal, and this may continue for some time. This tendency is more pronounced in successful cases, but also occurs to a lesser degree if there is no significant diuresis. The amount of protein in the urine frequently decreases, but its complete disappearance seems to be rare.

Relapse with recurrence of œdema may take place within a few weeks, although some patients have remained free from œdema up to twelve months. Relapse often follows a minor infection, usually of the upper part of the respiratory tract. After relapses, repetition of treatment may again cause remission, but this is not necessarily so. Conversely, if remission is not attained with a first course of treatment, further attempts may be successful.

Complications seem to be frequent. Sodium and water retention with pronounced increase in serous transudate may cause much anxiety. Paracentesis or even cessation of therapy may be necessary. Severe infections, particularly of subcutaneous tissues and the peritoneum, are not uncommon. Hypertension may be severe and cause cerebral vascular accidents.

There are very few reports as yet of the use of cortisone in this syndrome, but when used it does not appear to produce different results. The dosage advocated is 100 to 150 milligrammes daily, given either intramuscularly or in divided doses six-hourly by mouth.

The precise action of these hormones in the relief of the nephrotic syndrome is unknown. There is some evidence that while administration is continued the kidney regains its ability to secrete sodium in a similar fashion to that which occurs in spontaneous diuresis.

Juvenile Rheumatoid Arthritis.

Although there are many detailed reports on the action of corticotrophin and cortisone on rheumatoid arthritis in adults, little is yet available on their effect on this disease in childhood. In mild cases the older methods of treatment are probably just as effective for the present. In severe cases immediate relief of pain, stiffness, joint swelling and fever is the rule, with increase in weight and reduction of the anæmia. In order to maintain this improvement large dosage has to be continued for a fairly long time, in the hope that spontaneous remission will occur and that therapy will not again be necessary until recurrence takes place. Continued therapy is very likely to lead to side effects, and hyperadrenocorticism is almost inevitable. If the dose is reduced below a minimum, relapse is common. When joint deformity has resulted from the disease, and if this is not due to bony ankylosis, relief, can result from the administration of hormones. Joint movements become more free and physiotherapy can then be much more effective. If deformitics are developing in an acute case, administration of these drugs seems to be advisable. Whether this hormonal therapy will be of much use in other ways must await further study.

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Summary.

1. A minimal effective dosage of corticotrophin and cortisone is suggested when their use is indicated in childhood.

2. Common side effects are described and methods of early detection, prevention and treatment are mentioned.

3. The indications, dosage, results and examinations necessary when these hormones are used are described for rheumatic fever, acute leuchæmia, the nephrotic syndrome and juvenile rheumatoid arthritis.

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CORTISONE AND ACTH IN PÆDIATRICS.[1]

By R. H. VINES, M.R.C.P., M.R.A.C.P., D.C.H.,
Sydney.

FOUR years' use of cortisone and ACTH has given a greatly increased knowledge of their possible scope of employment. At the same time few conclusions on their final place in therapy are possible. My own experience and that of the Royal Alexandra Hospital for Children is so small that my remarks have been based on a review of the literature.

At present it appears that these drugs are highly indicated in the following conditions. (Adult dosage is given, as the requirements of children may be estimated from it.)

In adrenal cortical insufficiency adults require 100 to 300 milligrammes of cortisone per day during crises and 12·5 milligrammes twice a day for maintenance. Salt and DOCA are required in addition.

The use of cortisone in adrenal cortical hyperplasia marks a distinct advance. Wilkins has reported on eleven patients so treated. He recommends starting with intramuscular injections of 50 milligrammes per day of cortisone for older children and 25 milligrammes per day for infants. The 17-ketosteroid excretion must be depressed below eight milligrammes a day in the older group and below 1·1 to 1·7 milligrammes in infants. Maintenance doses are about 75 milligrammes given intramuscularly every third day, or from 25 to 75 milligrammes a day given orally in two to four divided doses for older children, and in infancy five to ten milligrammes a day given intramuscularly or two to three times as much given by mouth. It appears that this treatment needs to be continued for years, perhaps throughout life. Loss of acne, diminished hirsutism, breast development, regular menstruation and retardation of epiphyseal development have occurred with this *régime*. In several children who had hypertension associated with adrenal hyperplasia the blood pressure has been lowered. Infants with the salt-losing type of adrenal cortical hyperplasia need added salt and DOCA as well as cortisone.

Venning reported a case of adrenal cortical tumour in which cortisone failed to depress the 17-ketosteroid excretion. Perhaps this may later be found always to be the case with a tumour and so be a helpful test in distinguishing between neoplasm and hyperplasia.

[1] Read at a meeting of the Section of Pædiatrics of the New South Wales Branch of the British Medical Association on July 29, 1952.

In panhypopituitarism cortisone is a valuable addition to therapy.

A variety of inflammatory and allergic eye diseases are a very fruitful field for the use of these drugs. Sympathetic ophthalmia, syphilitic interstitial keratitis and optic neuritis in some cases are examples of conditions of general interest in which good results have been obtained. In retrolental fibroplasia most authorities consider the drugs are useless. Blodi *et alii* (1952) in a series of 32 cases found no benefit from the use of ACTH and had two deaths directly and four indirectly attributable to its use. Bembridge *et alii* (1952) have recently reported encouraging results in twelve cases. If these hormones are to be used, it must only be during periods of progression and in short courses.

In acquired hæmolytic anæmias there are many reports of good results, including a few in children. Either drug may be used, in the ordinary range of dosage, for a period of three weeks. If there is a recurrence, further courses may be effective and may be used to prepare the patient for splenectomy. Agglutinins may persist despite a satisfactory response.

Corticotrophin and cortisone have given excellent results in many hypersensitivity and toxic reactions, such as may occur with penicillin, sulphonamides, iodides, gold and atropine, and in serum sickness and exfoliative dermatitis. Cluxton (1951) has reported encouraging results in one case of snake bite and one of spider bite. A high dose is needed initially, followed by a two weeks' course.

Idiopathic hypoglycæmia has responded well to ACTH in six children. After a sustained course of ACTH maintenance has been possible with injections given twice a week. On the other hand, children with hypoglycæmia due to von Gierke's disease have shown very variable response.

In three rare and serious illnesses these drugs are indicated because we have no more effective therapy. Disseminated *lupus erythematosus* usually responds in acute phases, but maintenance with orally administered cortisone or long-acting ACTH is required. In *periarteritis nodosa* very high initial doses are needed to control the disease. They should be given early, but if renal involvement is at all pronounced, further deterioration may be caused. Less encouraging reports are the rule in dermatomyositis, but the drugs appear useful, especially if followed by a course of testosterone propionate. Even in childhood a daily dosage of 100 to 200 milligrammes of ACTH has been recommended in this disease.

In the same arbitrary fashion it may be said that in the next group of diseases ACTH or cortisone is to be regarded as indicated, at least in some cases. Thus Dr. Robertson has indicated their place in acute rheumatism, in rheumatoid arthritis and in the nephrotic syndrome.

There are a number of reports of good results in children with bronchial asthma, and it seems certain that the drugs will be valuable in this condition. Severe asthma usually responds well. Recurrence is usual when hormone therapy is stopped, and the condition may then be more severe than ever. A rather high dose is needed at first, and ACTH is to be preferred. In adults a course of 500 to 800 milligrammes given over at least ten days has been satisfactory. Courses of ACTH (five milligrammes daily for a three-year-old) and of cortisone (orally administered) have been given to ambulatory patients with moderately severe asthma by Glaser and others. Topical and inhalational use of cortisone also has given good results with relative economy. While at present most authorities would restrict their use to intractable *status asthmaticus*, it would seem likely that maintenance dosage on a domiciliary basis, with regular supervision, will be of great benefit to a few patients.

A similar but even more restricted field of usefulness would appear to be present in infantile eczema. This condition often responds well to hormone therapy, but relapse occurs quickly and occasionally shows a "rebound" exacerbation. Here again maintenance therapy would be desirable if only safe, small doses were sufficient. Usually they are not, so that the drugs are indicated only for the few

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patients who do not respond to conventional therapy, and who require only to be tided over a period of great severity of the disease.

The treatment of Rh-negative mothers with ACTH in the last two months of pregnancy is still in the experimental stage. Doerner reports two women so treated, one giving birth to an infant with *hydrops fœtalis* and the other to an affected infant who recovered with a simple blood transfusion and cortisone. Some improvement in the clinical and hæmatological picture of infants with erythroblastosis can be obtained with ACTH and cortisone, but it is also apparent that they will not be more than adjuncts to accepted forms of treatment.

In ulcerative colitis dramatic improvement may sometimes be obtained. This is chiefly subjective and symptomatic. Less frequently the sigmoidoscopic findings clear, and it appears to be quite unusual to find a reversal of the X-ray picture. Bleeding from the bowel may be exaggerated and relapse usually occurs on the suspension of treatment. The recommended course extends over four to eight weeks. Its place is in acute exacerbations and in the preparation of patients for surgery.

Variable, but some favourable, results have been reported in patients with regional enteritis.

After earlier discouraging reports there have been later most encouraging records of great improvement with the use of ACTH or cortisone in sarcoidosis. Too low a dosage appears to have been the reason for the first poor results. In view of the suspected tuberculous origin of this disease it will be interesting to see whether the development of frank tuberculosis is a hazard of such treatment.

Henoch-Schönlein purpura is said to respond well, unless there is associated nephritis. My own experience in this disease, limited to two cases, was disappointing. Thrombocytopenic purpura, idiopathic and otherwise, has remitted with ACTH and cortisone in some recorded cases. In some cases all findings have returned to normal and there has been no early relapse at least; in others, although the lesions have cleared, the platelet count has not risen and early relapse has occurred.

The administration of cortisone and ACTH to infected animals increases their mortality rate. Despite this, the use of these hormones in conjunction with antibiotics holds theoretical promise, and Forsham states that this promise is borne out in practice. General peritonitis, severe pulmonary infections and septicæmia have been so treated. The occurrence of unusual invasive infections during treatment with these hormones (for example, a monilial septicæmia described in an infant) and the increasing likelihood that an organism will prove resistant to antibiotics are obvious limitations to such therapy.

In meningococcal septicæmia the frequency of adrenal necrosis and hæmorrhage has suggested the use of cortisone for another reason—to replace the secretions of the damaged adrenals. There are few reports of such use, and evaluation will be very difficult. At the Royal Alexandra Hospital for Children there have been sufficiently encouraging results from this therapy to justify further attempts to evaluate it.

Hench has described the action of these drugs as that of "an asbestos suit behind which the patient protects his tissues from the fire". This simile is most literally applied to their use in the treatment of burns. A number of workers have reported great improvement in the appearance and general condition of patients so treated. Hume recommends starting with cortisone and changing to ACTH in forty-eight to seventy-two hours, and considers invasive infection likely if the administration is continued beyond two weeks. Warnings have been given about this treatment of burns. Complications appear to be many, and there may be serious deterioration on withdrawal of the drugs. Perhaps their use should be restricted to burns which are very likely to be fatal with conventional therapy.

Other possible fields of surgical usefulness lie in preparing the gravely debilitated for operation, in operations on patients with pituitary or adrenal disease, in allowing a short-time "take" of homografts, and in refractory shock with oliguria. In adults Ragan states that whereas 100 milligrammes of ACTH *per diem* cause only microscopic signs of retarded wound healing, 200 milligrammes *per diem* make this retardation obvious macroscopically. It is uncertain what dosage levels would make this effect important in pædiatric surgery.

In a last group of diseases benefit from these drugs is distinctly limited. Here I would include leuchæmia, Hodgkin's disease, lymphosarcoma, Letterer-Siwe disease, refractory anæmias, Cooley's anæmia, scleroderma, and hepatic disease. Beneficial results have been reported in all these diseases, but response is variable and generally not maintained.

Now, leaving the consideration of specific diseases in which the "glorified aspirin" has been used, I should like to pass on to more general aspects.

In the newborn a full response to ACTH is not obtained in the first week of life in all cases. ACTH and cortisone cause a negative nitrogen balance in infants and arrest weight gain and growth. This is followed by a comparable period of excessive gain in weight and length on withdrawal. For the first two months of life ACTH causes sodium loss, instead of retention, and this may be serious if long continued. Infants given more than five milligrammes per kilogram of ACTH per day show irritability, hyperactivity and a ravenous appetite. Blanching, often occurring after ACTH injections, has been ascribed to the presence of posterior pituitary principle as a contaminant. With continued administration tachycardia, hypertension, œdema, papular skin eruptions, regurgitation, a Cushing facies, hypokalæmia, convulsions and sudden death and invasive infections have all been seen. At post-mortem examination of at least two infants an enlarged heart, enlarged liver and nephrocalcinosis have been found. It is apparent that there are considerable dangers in treating young infants with ACTH or cortisone and that prolonged administration of these agents is to be avoided.

It is important to select the right drug in many cases. In adrenal insufficiency, in panhypopituitarism and in adrenal hyperplasia cortisone must be used. In the first week of life cortisone may be more reliable, though many good results have been claimed with ACTH. Topically and orally only cortisone can be used. Allergic reactions and insensitivity to ACTH occur occasionally, especially with repeated courses. ACTH leaves less adrenal depression on discontinuance. Moreover, in this country it is more readily available and to be preferred for that reason.

Subcutaneously or intramuscularly, ACTH is given every six to eight hours. Long-acting preparations in oil or gelatin given once or twice a day are in use in America. Twenty milligrammes given intramuscularly by the "drip" method over eight hours give maximal adrenal stimulation in an adult. If the infusion is continued longer, less is required.

Intramuscularly, cortisone need be given only once or twice a day after the first one or two days, but when it is given orally the effect is more rapidly obtained and transient, so that it must be given every six to eight hours. When it is given orally, 1·2 to 1·5 times the intramuscular dose is usually required.

A phase of adrenal depression occurs two to four days after withdrawal of ACTH and seven to ten days after the parenteral administration of cortisone has been stopped. An adrenal crisis may occur then if stress is sufficiently great.

In adults the dose of ACTH is usually between 40 and 160 milligrammes per day. Forsham states that two and a half times these doses of cortisone given intramuscularly are equivalent.

In the assessment of dosage the clinical response is the final criterion. Oxycorticoid and 17-ketosteroid estimations are impracticable tests for routine assessment of effective dosage. The eosinophile cell count is of value; 80% to 90% depression is usually obtained with effective doses, but such depression may fail to occur with cortisone given by the intramuscular route and in allergic eosinophilia, while in other cases it is too delicate a response and will

XUM

be achieved with an inadequate dose. If the amount is assessed on a weight basis, children tend to require a rather higher dose than adults.

In giving these substances certain precautions should be observed, such as the following: (i) Careful clinical observation is required, including daily weighing and urine testing and a close watch for signs of infection or gastro-intestinal disorder. (ii) Preliminary Mantoux testing and electrocardiography should be carried out whenever possible. (iii) Dietary measures, such as salt restriction, an increased protein intake and the administration of two to six grammes of potassium chloride per day, should be observed. (iv) Frequent blood pressure estimations should be made. (v) Selected special tests should be carried out—for example, leucocyte counts, electrocardiography, plasma protein estimations, and fasting blood sugar estimations. I have included these special tests as necessary precautions, as they can give warning of overdosage and can be performed in any hospital. In selecting the appropriate test, for example, one would make leucocyte counts in the first few days, as severe neutrophile leucocytosis with extreme depression of lymphocytes would be good evidence of overdosage. Plasma protein or chloride depression and elevated blood sugar levels would be better evidence later, while a weekly electrocardiogram is certainly advisable if potassium salts are not being given. With prolonged administration of small doses of ACTH and cortisone these precautions may be relaxed, but close clinical observation still remains essential.

Apart from the well-known signs of hyperadrenocorticism—the moon face, striæ, hirsutism, acne *et cetera*—there are several complications of particular importance in children. These are the not infrequent occurrence of invasive infections, the development of hypertension (in over a third of one series) and the onset of convulsions which have occasionally led to death or irreversible damage to the nervous system. Pædiatricians, too, will be interested in the production of cleft palates and other deformities in the offspring of pregnant rats given ACTH, as reported by Fraser and Fainstat.

Conclusion.

In conclusion, I want to emphasize that this paper is based on a review of an inadequate though voluminous literature. It is apparent that the best results are obtained in certain rare conditions. In the commoner conditions in which ACTH and cortisone are of value, their use is limited by the transience of the benefit obtained and by the serious nature of the complications which may occur. These complications make their use unjustifiable unless the precautions mentioned are put into practice.

Summary.

1. A brief account of the clinical use of corticotrophin and cortisone in pædiatrics is presented.
2. Precautions necessary in the use of these drugs are suggested.

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OBSERVATIONS ON VIRUS ENCEPHALITIS IN SOUTH AUSTRALIA.

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IN January and February of 1951 there was a sharp outbreak of encephalitis along the River Murray and at the same time a few cases of encephalitis occurred in areas away from the river. The isolation of a virus from a fatal case in Victoria was reported in an article on the epidemic by the workers at the Walter and Eliza Hall Institute (1951) and from an isolated fatal case in an area 75 miles north of Adelaide by Miles, Fowler and Howes (1951). The two viruses have been found to be identical by both groups (French, 1952; Miles and Howes, 1952). The Melbourne workers have described the Murray Valley outbreak in a series of papers in THE MEDICAL JOURNAL OF AUSTRALIA (Anderson, 1952; French, 1952; Robertson and McLorinan, 1952; Robertson, 1952; Anderson *et alii*, 1952). The strain of virus isolated in South Australia is described in two papers (Miles, 1952; Miles and Howes, 1952). French and ourselves both conclude that the virus isolated is related to the Japanese B group of viruses, but sharply distinct from any of the previously described members of the group.

Because of the clinical picture of the disease, the histological appearances in fatal cases from this and previous outbreaks, the range of pathogenicity for experimental animals, the clinical picture in such animals and the histological changes found in their brains, we are of the opinion that this epidemic represents a recurrence of Australian "X" disease, and we shall present meteorological data to suggest that an epidemic of "X" disease was to be expected in the summer of 1950-1951.

In this communication we shall report our investigations on the disease in this State and the results of researches into the weather reports of the last forty years.

Materials and Methods.

The specimens of human serum were obtained through the cooperation of medical practitioners in the areas concerned. The horse sera were mainly collected by the officers of the Livestock Division of the Department of Agriculture. The bird sera were collected in the field from birds shot.

The techniques of the complement fixation and neutralization tests used in this investigation are described in detail elsewhere (Miles and Howes, 1952).

Results.

In this State only one case of encephalitis due to the virus of the Murray Valley epidemic has been completely proved. This was the fatal case in which the virus was isolated from the subject's brain. In three other cases of encephalitis which occurred in January or February, 1951,

[1] Assisted by a grant from the National Health and Medical Research Council.

TABLE I.

Results of Serological Testing of Human and Horse Sera in South Australia.

Area.	Numbers of Sera.									
	Human.					Horse.				
	Tested by Complement Fixation Test and Neutralization.			Additional Results with Negative Complement Fixation Test Only.	Total Percentage Positive Results.	Tested by Complement Fixation Test and Neutralization.			Additional Results with Negative Complement Fixation Test Only.	Total Percentage Positive Results.
	Total.	Positive Results.	Percentage Positive Results.			Total.	Positive Results.	Percentage Positive Results.		
Metropolitan ..	134	2	2	219	<1	8	0	0	4	0
Central	51	5	*	6	*	50	7	*	12	*
Murray Valley ..	53	15	28	22	20	29	20	69	3	63
South	38	1	*	4	*	2	0	0	3	0
South-east ..	34	3	*	8	*	9	0	0	9	0
North	32	3[1]	*	39	*	—	—	—	16	0
West	29	1	*	2	*	4	1	25	5	*
Northern Territory	40	11	27	2	26	—	—	—	—	—

[1] In one of these cases the object had recently moved into the area from Queensland.

* Numbers too few to allow percentages to be taken.

after the patients' recovery high-titre complement-fixing and neutralizing antibodies against the virus were found. Two of these were from one town in the Murray Valley; the third, like the fatal case, was from the area which we shall refer to as central South Australia (Figure I). No evidence was obtained of any unusual morbidity or mortality among horses or dogs.

A serological survey has suggested that infection with the virus was more widespread than the number of clinical cases had suggested. At first the complement fixation test was used alone, except on sera which were of exceptional interest or which gave a positive result to the complement fixation test. On these a neutralization test was also performed.

After a time it became clear that many sera giving a positive result to neutralization tests gave a negative response to the complement fixation test. Anderson *et alii* have shown that the sera of people who were "seropositive" after an inapparent infection gave a negative response to the complement fixation test after a few months. Also we found direct experimental evidence that, at least in horses, the complement-fixing antibody was less long-lasting than the neutralizing antibody. Since this has been shown to be true with human sera in the case of Japanese B (Hammon, 1948), and since we obtained twice as many positive results by neutralization tests (Miles and Howes) as by complement fixation tests with both horse and human sera, both tests were used on all sera received after the importance of the neutralization test had been established.

For the purposes of this investigation we have used an unusual subdivision of the State (Figure I and Table I). The "Central" area is roughly the area north of Gawler, east and north of the Murray and south of Port Augusta. The Murray Valley is a strip 20 miles wide along the River Murray and around Lake Alexandrina. "South" is the area south of Gawler and east of the Murray, including Yorke Peninsula. "North" is north of Port Augusta, and "West" is west and south of Port Augusta.

Because of the movement of human populations, small percentages of positive serum findings cannot be regarded as significant, and Bawell *et alii* (1951) have suggested in the case of Japanese B that it is not safe to regard a percentage of human positive results lower than 5·0 as giving evidence of infection in any area.

Anderson *et alii* have found a much higher percentage of horse than human sera to give positive results in Victoria, and our figures suggest that the same is true in South Australia. Further, the movements of horses are better known and more restricted than those of their owners, so the presence or absence of antibodies in horses may be used to confirm the results on human sera. On this basis the two positive neutralization test results from the metropolitan area can be neglected, and we can state that we have no definite evidence of infection in the metropolitan area, the south or the west. The few horse sera tested in these areas gave negative results except for one from the west. From the north many sera were tested only by complement fixation, and one of those giving positive results had recently arrived from Queensland. We do not think that the three positive results constitute a strong case for thinking that infection has taken place to any extent in this area, especially when the 16 horse sera tested all gave negative responses to the complement fixation test. However, one of 16 bird sera from this area was positive.

In the south-east three human sera giving positive results were found in an investigation of 42 human sera and none among 18 horse sera. Only the investigation of a larger series would enable us to decide definitely whether infections had been taking place in this area.

In the central area virus was isolated from one case, and serological evidence from both men and horses shows that infection occurred widely over the area, but not very commonly. In the Murray Valley infection was very common, but our figures cannot be compared directly with those of Anderson *et alii* because about half our sera giving positive results reacted only in the neutralization test and gave a negative response to the complement fixation test, the only test these workers used.

Particularly interesting are the results with a small collection of sera from aborigines in the Northern Territory. These showed as high an infection rate as human sera from the Murray Valley, and they provide an interesting comparison with the sera investigated by Anderson *et alii* from Mornington Island in the Gulf of Carpentaria and from towns in other parts of Queensland. To us they suggest the possibility that the disease may be endemic in the Northern Territory and in Queensland.

Birds.

Since this virus has been shown to be related to the Japanese B group, it was reasonable to suspect that the natural history of the disease was comparable. Both Japanese B and St. Louis viruses in Nature infect wild birds and may be regarded as primarily a disease of such birds, while St. Louis virus may be transmitted from bird to bird either by mites (mainly of the Dermanyssus group) or by mosquitoes (Hammond Reeves, 1943; Smith, Blattner and Heys, 1944). They may be transmitted to mammals and man by those mosquitoes which will bite both birds and mammals.

We have therefore made a limited survey of bird sera for the presence of antibodies against the virus.

Because many bird sera will not fix guinea-pig complement, we have used only the neutralization test on the bird sera (Table II).

Sera from 20 land birds from the central area—parrots, crows and magpies—all gave negative results. Twenty-five Anseriformes (ducks and swans) from the Murray and lakes in the north gave five positive results, and 24 Ralliformes (water-hens *et cetera*) also gave five positive results. Eleven Pelecaniformes (cormorants and darters) gave only one positive result. The one blue crane (*Notophoyx novæ-hollandiæ*) tested gave a positive result, and one silver gull (*Larus novæ-hollandiæ*) gave a negative result.

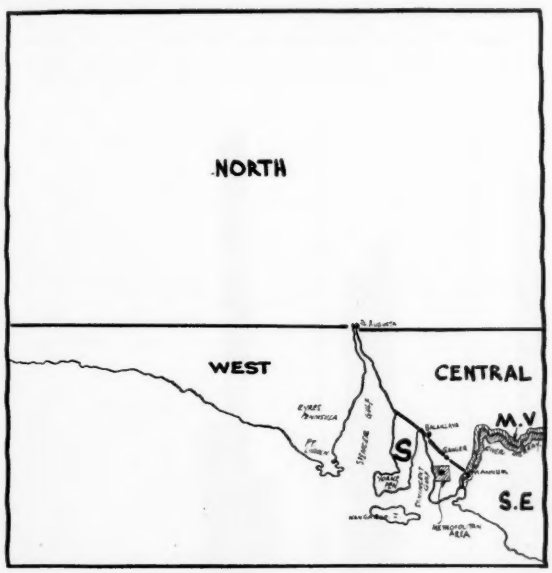

FIGURE I.
Map of divisions of South Australia.

In all, 46 sera from the Murray Valley gave 11 positive results, 16 from the north gave one positive result, and there were no positive results among the 20 land birds from the central area.

Among those birds which showed definite juvenile plumage there were no positive findings. Unfortunately the maturity of the ovaries or testes in the others was not examined, but such evidence as we have from the birds confirms the impression gained from the absence of clinical cases of encephalitis in the summer of 1951-1952 that the virus was not present in South Australia at that time.

Past Epidemics.

Three epidemics of "X" disease have been reported. In the summer months of 1916-1917 and 1917-1918 there were epidemics mainly in New South Wales, but also a group of cases occurred in the Goulburn Valley in Victoria in 1918 (Cleland, Campbell and Bradley, 1917). In 1924-1925 there was a small outbreak with nine cases at Broken Hill, which had been badly hit by both the previous outbreaks, and one elsewhere (Kneebone and Cleland, 1926). Nearly all the cases in all epidemics occurred between January and April, the peak of the epidemic being in either February or March.

There is no evidence that the disease occurred in south-eastern Australia except in the known epidemic years, and apparently there was a gap of twenty-six years between 1925 and 1951. Since physicians have always been on the alert for a recurrence of "X" disease, it is unlikely that any outbreak has been missed. A small outbreak of encephalitis did occur in the Northern Territory in the spring of 1943. This was reported by Horan *et alii* (1944), but was not the same as "X" disease. Other cases of obscure central nervous system lesions do occur in the Northern Territory of Australia.

Since antibodies are present in quite a high percentage of the sera tested from Northern Territory and Queensland in the absence of a recent epidemic, and since epidemics are very unusual in south-eastern Australia and sporadic cases are certainly rare apart from epidemic years, it is natural to postulate that the disease is primarily a disease of wild birds in the sparsely populated northern areas,

TABLE II.
Results of Testing Bird Sera.

Group of Birds.	Number Tested.	Number Giving Positive Results.
Anseriformes (ducks *et cetera*)	25	5
Ralliformes (water-hens)	24	5
Pelecaniformes (cormorants and darters)..	11	1
Land birds	20	0
Notophoyx novæ-hollandiæ (blue crane) ..	1	1
Larus novæ-hollandiæ (silver gull).. ..	1	0
Total	82	12

where there is insufficient human population to support an epidemic, and that only under exceptional circumstances does the disease appear in the south in areas where there is a considerable human population. The virus would presumably be brought from the north by infected birds (we

TABLE III.
Number of Meteorological Districts in Northern Territory, Northern South Australia and Queensland having Above Normal Rainfall between August and January in Years 1913 to 1937 and in 1950 to 1951.

Period: August to January.	Total Number of Districts Above Average Rainfall.[2]	Northern[3] and Central Districts.	Queensland.[4]
1913–1914	7	4	3
1914–1915	3	3	0
1915–1916	6	1	5
1916–1917	22	4	18
1917–1918[1]	21	2	19
1918–1919	1	0	1
1919–1920	4	2	2
1920–1921	13	3	10[5]
1921–1922	9	0	9
1922–1923	2	2	0
1923–1924	1	1	0
1924–1925[1]	21	3	18
1925–1926	4	0	4
1926–1927	3	0	3
1927–1928	5	0	5
1928–1929	8	0	8
1929–1930	4	0	4
1930–1931	7	3	4
1931–1932	8	0	8
1932–1933	3	1	2
1933–1934	17	1	16[5]
1934–1935	6	1	5
1935–1936	3	2	1
1936–1937	5	4	1
1950–1951[1]	23	4	19

[1] Epidemic years.
[2] Twenty-three districts investigated: Bureau of Meteorology numbers 14 to 17 and 27 to 45.
[3] Districts 14 to 17 Northern Territory and northern South Australia.
[4] Districts 27 to 45 Queensland.
[5] No abnormal rainfall in district 29.

have shown that some birds may carry virus in the blood for over a week). Such birds could then infect mosquitoes in the area in which they arrived, which in turn could then infect further birds (leading to an epizootic in the wild bird population), and when the concentration of infected birds had risen sufficiently high, man and his domestic animals would also become infected. It appears

certain that some dispersal of birds from breeding grounds in the north occurs every year. It is probably mainly a dispersal rather than a true migration. In certain years the number of birds coming south is exceptionally large. This was true of the summer of 1950-1951, and many birds which must have been bred further north, in the absence of good rains in the north, have stayed in southern areas.

Serventy and Whittell (1951) have shown very clearly that in Western Australia the breeding of birds is not dependent on the time of year, but rather on the occurrence of rain. Those observers who have spent a considerable time in the north in places where there is a genuine dry season agree that this is also true in such parts. They also hold that in good seasons two or more broods are raised by many species. The dates of collection of eggs of water birds from the Northern Territory in the collection at the South Australian Museum extend from October to June—nine months of the year.

We have, therefore, examined meteorological data from the Northern Territory and Queensland, on the theory that the most important factor in causing epidemics might be exceptional and widespread early rains in the endemic areas, leading to early and exceptional breeding of both birds and mosquitoes and a consequent dispersal of infected birds driven out at the time of the second brood.

It seemed likely that if the disease was to reach the south-east, the breeding of a large population of susceptibles over a wide area would be necessary.

Meteorological Data.

We have had available Australian rainfall district averages from 1913 to 1937, and more detailed information about parts of Queensland up to 1940 and parts of New South Wales up to 1945. We have also received the district averages from the Northern Territory, lower Carpentaria, trans-Darling south in New South Wales, and the Murray district, which includes Mildura, up to the end of 1951, and also the district averages for Queensland for the years 1950 and 1951.

Table III shows the results of analysing the district rainfalls for the Northern Territory, for the north of South Australia, and for Queensland from 1913 to 1937 and for 1950 and 1951. In this area there are 23 districts and we have enumerated the number of districts which had a rainfall more than 10% above the average for the period August to January. It will be seen that in the three epidemic years either 21 or 22 of these districts had above-average rainfall in this period, and that the two non-epidemic years with the most widespread high rainfall showed a rainfall above average in 17 and 13 districts respectively. In no other years were there more than nine districts with a rainfall above average. In 1950-1951 all 23 areas showed above average rainfall, and very many stations in eastern and northern Australia recorded their record rainfalls in the year 1950.

Figure II shows the mean rainfall for lower Carpentaria (which includes Mornington Island) for the four epidemic years. It will be seen that in each year there was a very high rainfall in spring and early summer, and that the peak in December-January is earlier than the usual, which is in February. In Table IV the actual figures are shown, and also those for the two non-epidemic years with the most widespread high rainfall during the early part of the season. In this particular area the four epidemic years are the four years with the highest early rainfall in the records for thirty-nine years available to us.

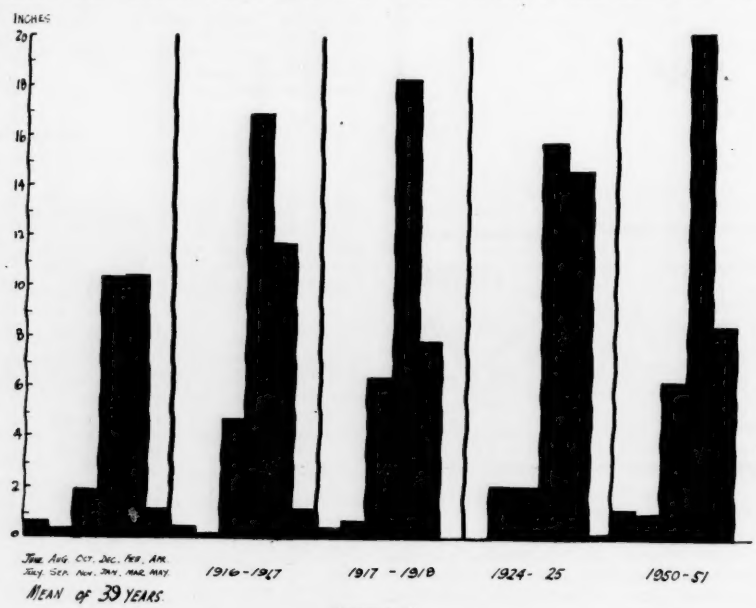

FIGURE II.

Rainfall in lower Carpentaria district: *mean of thirty-nine years and in the encephalitis years*

The average rainfall over the whole area considered was in the three main epidemic seasons 1916-1917, 1917-1918 and 1950-1951 above that in any of the non-epidemic years for which we have the figures (Table V). The average for 1924-1925, in which there were only a few cases at Broken Hill, was almost exactly the same as that for the non-epidemic year with the highest rainfall, 1933-1934. The main difference between the two years lay in how widespread the high rainfall was. It is also possible that the difference in the lower Carpentaria district was of significance.

By contrast to the northern areas, in those areas in which the epidemics actually occurred the seasons have not been so abnormal (Tables VI and VII). In the three years in which there were cases at Broken Hill there was a rainfall well above average in the months preceding the epidemic, and presumably there was plenty of water about to allow mosquito breeding and to attract water birds. It is perhaps noteworthy that in 1950-1951, in which there

were no cases at Broken Hill, there was no excess rainfall between June, 1950, and May, 1951, in that district.

In the Mildura region, which was spared in the first three epidemics, the rainfall before the epidemic season was high in all those years, but not in 1950-1951 when the actual epidemic occurred (Table VII). However, the water supply in that region is dependent more on the rainfall at the sources of the Murray and Darling than that on the spot, and adequate mosquito breeding must occur every year. The problem is not why the epidemic hit that region in 1950-1951, but why it and other apparently suitable areas were spared in the other years.

Conclusion.

As a result of these investigations we propose the following tentative theory of the epidemiology of this disease.

The virus is a virus of wild birds, in which it normally causes a mild non-fatal disease with either brief or fairly prolonged viræmia. We may hazard a guess that it may be spread between birds either by mites or by mosquitoes. In seasons with exceptional early rains, when birds breed early and second broods are usual, early movements of young birds to the south occur; many of these birds may be infected, and when they arrive at suitable destinations in the season when mosquitoes and susceptible juvenile

TABLE IV.

Rainfall District 29 (Lower Carpentaria).[1]

Year.	June-July.	August-September.	October-November.	December-January.	February-March.	April-May.
1916–1917[2]	41	11	464	1,678	1,171	118
1917–1918[2]	28	58	630	1,820	882	3
1920–1921	142	4	294	856	1,198	511
1924–1925[2]	1	204	206	1,569	1,450	12
1933–1934	148	22	188	1,119	586	105
1950–1951[2]	107	88	620	2,011	842	1
Mean for 39 years	72	30	189	1,029	1,035	116

[1] One hundred points equal one inch of rain.
[2] Epidemic years.

TABLE V.

Mean Rainfall in Epidemic Years, the Highest Rainfall in Non-Epidemic Years, and the Average of 24 Years for the 23 Districts Investigated.[1]

Year.	Rainfall.						
	Epidemic.	August.	September.	October.	November.	December.	January.
1916–1917	Yes.	91	78	240	346	713	666
1917–1918	Yes.	122	205	120	508	480	1,108
1920–1921	No.	94	118	193	217	394	578
1924–1925	Yes.	136	107	175	381	411	582
1933–1934	No.	85	150	177	443	424	534
1950–1951	Yes.	40	64	281	540	509	858
Mean of 24 years	——	54	76	111	184	472	527

[1] One hundred points equal one each.

TABLE VI.

Rainfall District 47 (Trans-Darling, South New South Wales).

Year.	June-July.	August-September.	October-November.	December-January.	February-March.	April-May.
1916–1917[2]	370 (385)[3]	395 (322)	268 (217)	309 (364)	349 (341)	72 (54)
1917–1918[2]	337 (287)	336 (310)	434 (341)	103 (163)	95 (74)	436 (484)
1920–1921	144 (184)	426 (489)	331 (318)	146 (78)	498 (530)	323 (340)
1924–1925[2]	103 (48)	203 (156)	231 (232)	185 (254)	186 (122)	219 (256)
1933–1934	79 (69)	157 (90)	464 (486)	146 (149)	84 (98)	41 (43)
1950–1951[2]	191	41	193	137	39	90
Mean for 39 years (56 years)	167 (170)	144 (141)	165 (153)	133 (141)	169 (142)	145 (157)

[1] One hundred points equal one inch of rain.
[2] Epidemic years.
[3] Figures in parentheses are those for Broken Hill.

TABLE VII.

Rainfall District 76 (Mallee North, Victoria).[1]

Year.	June-July.	August-September.	October-November.	December-January.	February-March.	April-May.
1916–1917[2]	356	553	399	135	355	189
1917–1918[2]	333	547	543	101	205	456
1920–1921	203	586	417	304	387	214
1924–25[2]	142	312	462	154	164	208
1933–34	192	273	197	305	112	107
1950–51[2]	128	205	276	104	37	192
Mean for 39 years	220	218	208	141	167	188

[1] One hundred points equal one inch of rain.
[2] Epidemic years.

locally bred birds are numerous, they initiate an epizootic. When, either by direct flight or through a chain of infection arising from shorter dispersal flights, the birds initiate an epizootic in a more densely settled area, man and his domestic animals may be casually infected. The exact area in which the epidemic occurs will depend on the arrival of infected birds at a time optimal for spread of the disease.

We also suggest that observation of the weather reports for the Northern Territory and Queensland for the months from October to December will give a warning of any year in which an epidemic is likely to occur.

Acknowledgements.

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Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Surgery of the Œsophagus", by R. H. Franklin, M.B., B.S., F.R.C.S.; 1952. London: Edward Arnold and Company. 9″ × 6″, pp. 234, with 86 illustrations. Price: 42s.

Primarily for the general surgeon.

"The Change of Life and its Problems", by Lilias Blackett Jeffries, M.D., B.S. (London); 1952. London: Victor Gollancz, Limited. 7½″ × 5″, pp. 136. Price: 4s. 6d.

The author writes from personal experience.

"Physical Foundations of Radiology", by Otto Glasser, Edith H. Quimby, Lauriston S. Taylor and J. L. Weatherwax; Second Edition; 1952. New York: Paul B. Hoeber, Incorporated. 7½″ × 5½″, pp. 594, with 112 text figures. Price: $6.50.

For the medical practitioner and student. The previous edition was published in 1944.

"Aids to Organic Chemistry for Medical Students", by Ian Leslie, B.Sc., Ph.D., with an introduction by R. H. A. Plimmer, D.Sc.; Fourth Edition; 1952. London: Baillière, Tindall and Cox. 6½″ × 4½″, pp. 152. Price: 5s.

One of the well-known "Aids" series. The author aims "to give just the information that is necessary to the understanding of biochemistry".

"The Science and Practice of Surgery", by W. H. C. Romanis, M.A., M.B., M.Chir. (Cantab.), F.R.C.S. (England), F.R.S. (Edin.), and Philip H. Mitchiner, C.B., C.B.E., T.D., M.D., M.S. (London), F.R.C.S. (England), D.Ch. (Durham), M.Ch. (Cairo); Ninth Edition; 1952. London: J. and A. Churchill, Limited. In two volumes. Volume I: General Surgery. 9½″ × 6½″, pp. 880, with 20 plates and 402 text figures. Price: 32s. Volume II: Regional Surgery. 9½″ × 6½″, pp. 1026, with eight plates and 326 text figures. Price: 36s.

Fully revised and partly rewritten since the previous edition was published in 1948.

"Textbook of Surgery", edited by H. F. Moseley, M.A., D.M., M.Ch. (Oxon.), F.A.C.S., F.R.C.S. (England), F.R.C.S. (C.). with a foreword by G. Gavin Miller, M.D., C.M., M.Sc., F.R.C.S. (C.), F.A.C.S.; 1952. St. Louis: The C. V. Mosby Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 10″ × 7½″, pp. 918, with 46 plates in colour and 460 text figures. Price: £7 17s. 6d.

Primarily for medical students and recent graduates. The contributors are nearly all on the staff of McGill University, Montreal.

"Synopsis of Obstetrics", by Jennings C. Litzenberg, B.Sc., M.D., F.A.C.S.; Fourth Edition; 1952. St. Louis: The C. V. Mosby Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 8″ × 5½″, pp. 378, with 157 illustrations, five in colour. Price: £2 17s. 9d.

Primarily for the medical student.

"Laboratory Technique in Biology and Medicine", by E. V. Cowdry; Third Edition; 1952. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 9″ × 6½″, pp. 414. Price: 48s. 6d.

The previous edition was published in 1948.

"Operative Neurosurgery: With Emphasis on Procedures in Trauma", by Elisha Stephens Gurdjian, M.D., and John E. Webster, M.D.; 1952. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 10½″ × 7″, pp. 436, with 129 illustrations. Price: £5 7s. 6d.

The author aims to give "pertinent anatomic, diagnostic, and technical information in the execution of certain operative procedures in neurological surgery".

"A Method of Anatomy: Descriptive and Deductive", by J. C. Boileau Grant, M.C., M.B., Ch.B., F.R.C.S. (Edin.); Fifth Edition; 1952. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 10½″ × 7″, pp. 894, with 862 text figures. Price: 75s. 3d.

Fully revised with addition of new material but no increase in size.

The Medical Journal of Australia

SATURDAY, JANUARY 3, 1953.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: surname of author, initials of author, year, full title of article, name of journal without abbreviation, volume, number of first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

A NEW MEDICAL RESEARCH FUND FOR AUSTRALIA AND NEW ZEALAND.

THE year 1953 will be marked by the inauguration of a new medical research fund for Australia and New Zealand. It is a fund for which many have been hoping and waiting for years, but for which a few ardent souls have been working quietly for some considerable time. For many years now, life assurance societies in the United States of America have undertaken medical investigations and have fathered research which has yielded important results. It is a common-sense point of view for life assurance societies to adopt, for, if the causes of disease can be discovered and the lives of policy-holders prolonged, the financial position of the companies will be improved and the policy-holders will reap the benefit. The Life Offices' Association for Australasia has established a fund for the promotion of scientific and medical research in Australia and New Zealand. We understand that the proposal at present is to spend something like £25,000 *per annum*. The capital sum represented by such an annual expenditure is far from inconsiderable. It is intended, for a start, that the resources of the fund will be used to stimulate and support research in the function and diseases of the cardio-vascular system. It is well known that diseases of the cardio-vascular system are the commonest cause of death. We read in the "Year Book of the Commonwealth of Australia" for 1951 that the number of deaths for 1948 for the whole of Australia was 76,839, or 9965 per million. Diseases of the heart accounted for 24,262 deaths, or 3146 per million; intracranial lesions of vascular origin accounted for 8310 deaths, or 1078 per million, and other diseases of the circulatory system for 2060 deaths, or 267 per million. The total is 34,632 deaths, or 4491 per million. The Year Book also tells us under the heading of "Life Assurance" that in 1948 there were in existence in Australia 2,070,939 insurance and endowment policies. The sum for which assurances were effected was £834,467,000. The annual bonus additions were £92,704,000; the annual premiums were £28,767,000. While, therefore, the Life Offices' Association of Australasia is to be congratulated upon the common-sense step which it has taken, it is clear that they have done something which they can well afford to do—they are spending less than 0·09% of their premium income in this endeavour. There can be no doubt that the research to be fathered by this fund will help with other research projects to make the span of life in Australia and New Zealand still longer than it is. Unfortunately, it will be impossible to point categorically to certain results as having justified the expenditure of money on research, unless indeed some epoch-making discovery should be made. This is never beyond the range of possibility. From the life assurance point of view the importance of this innovation may be estimated by the fact that there are over two million policies in existence in the Commonwealth. One well-known Australian assurance office claims that it is represented in one of every three homes in the Commonwealth.

Grants from the fund will be made either as grants-in-aid to institutions or as research Fellowships. Grants-in-aid will be made by the committee of management on the recommendation of an advisory council. The Advisory Council will be as follows: Dr. A. W. Holmes à Court, Dr. R. S. Aitken, Sir Macfarlane Burnet, Dr. F. C. Courtice, Professor H. R. Dew, Dr. Ewen Downie, Dr. C. H. Fitts, Dr. John H. Halliday, Dr. M. R. Lemberg, Dr. C. G. McDonald, Sir David Rivett. The chairman of the Advisory Council will be Dr. S. A. Smith. Dr. John H. Halliday will be Medical Director of the fund. Grants-in-aid will be made only to non-profit institutions which have the requisite basic facilities for research. A grant will be made on condition that the sum awarded is used in support of a particular research programme which has been submitted by the head of the department or institute concerned who is the responsible investigator for the grant. As a rule, grants will be made for programmes which require between £1000 and £3000 per year. In special circumstances larger grants may be made. It is not intended to make grants which will merely supplement programmes that are receiving support from other sources. In accordance with the needs of the individual programme, the sum granted may cover salaries for research or technical assistance and secretarial work directly involved, the costs of supplies, animals, special equipment, and other necessary expenses including a reasonable amount for travel connected with the research. The salary of the responsible investigator must be provided from other sources, and must be reasonably assured for the duration of the grant. Grants-in-aid will be made for periods of one, two, or three years, and all results from work supported by the fund are to be made available for publication in scientific journals. One excellent provision is that any discovery arising as the result of work supported by the fund shall not be subject to patent, except with the written approval of the authorities of the fund. Approval in such circumstance may be given when the best interests of the public will be served by such a procedure, and even then, the filling in of an application for a patent will be approved only under conditions in which no financial profit will accrue to the inventor, the institution, or the fund.

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Research Fellowships will be available to medical graduates or to those with equivalent scientific training between the ages of twenty-three and thirty-five years. In special circumstances, applicants outside these age limits may be considered. Two types of Fellowships will be awarded, those tenable in Australia and New Zealand, and those tenable overseas. Fellows will be expected to devote their full time to research under the supervision of an experienced investigator. Holders of Fellowships in Australia and New Zealand will receive from £1250 to £1500 *per annum*. Fellowships will be awarded for a period of twelve months, and may be renewed for further periods on the recommendation of the Advisory Council. Renewal of a Fellowship will carry an increased remuneration of £150 *per annum*. Fellowships overseas will be granted for a period of three years. Of these, two will be spent abroad and the third in an approved institution in Australia or New Zealand. These provisions will meet with general approval since they will be likely to result in an increase in the number of research workers resident in Australia and New Zealand. The awards will range from £1500 to £2000 *per annum* and approved travelling expenses will be allowed. The same provisions in regard to publication and patents apply to Fellowships tenable overseas as to those tenable in Australia or New Zealand. A sum up to £150 *per annum* will be paid to the institution in which the research is carried out in order to help to defray the laboratory expenses incurred in connexion with the Fellowship. Provisions have been made for a further type of senior Fellowship which will be awarded under conditions to be recommended by the Advisory Council. The intention is that, under this provision, it will be possible to bring to Australia or New Zealand some prominent investigator whose work may have been held up or completed and whose services might not otherwise be made available to this part of the world. It may seem advisable also to appoint as senior Fellow some distinguished Australian or New Zealand investigator of senior rank who might not otherwise be able to continue his work.

There is every reason for great satisfaction and enthusiasm over the creation of this fund. To begin with, although the study of cardio-vascular function and disease covers an enormous field, we may take it that the scope of work to which approval will be given will eventually be extended beyond this. In the Education Number of this journal which was published last November, stress was laid on the importance of research in medical education and also on the need for the recognition and shepherding of students with first class minds. Those who administer this fund will be able to do something to further desirable objectives in post-graduate medical education at the same time as they are seeking for ways and means to mitigate the ravages of cardio-vascular and other diseases. At the present time there is a gap which sometimes makes it necessary for research workers of promise to abandon research in order to find bread and butter for their families in the more lucrative field of medical practice. It has been stated here that the work envisaged will bring added revenue to life assurance companies and benefit to the holders of life insurance policies. It will, of course, do more than this, for every increase in the knowledge of disease must, in the long run, benefit the whole community. A final point, not without value, is that another link has been forged in the chain which binds medicine in the Commonwealth of Australia with medicine in its sister Dominion of New Zealand.

Current Comment.

THE SURGICAL TREATMENT OF MITRAL STENOSIS.

PERHAPS the aphorism of a celebrated surgeon that "a surgeon was a physician doomed to the practice of surgery" might be varied today, for he appears, like the physician, to need more and more to be a practical physiologist. There was a time when mitral regurgitation faded out of the diagnostic picture and the whole emphasis was placed on mitral stenosis. This was a revulsion from the older days, when the detection of a bruit apparently arising from the mitral valve automatically caused concern, but now it seems as if true physiological principles have adjusted the point of view in mitral lesions, and both stenotic and regurgitant lesions have their right place. The surgeon has really been responsible for this more balanced attitude; indeed, it has been forced on him by the recognition that when by his skill he relieves the constriction of the mitral opening he may produce an unwelcome degree of insufficiency. Further, it is curious that, while his informed finger-tip may not only detect the presence of a regurgitant jet but also be able to make a rough estimate of its degree, if more accurate assessment is desired it is necessary to use a highly technical method which gives qualitative but not necessarily quantitative answers. This is one of the many variables which affect the result of operation, and the selection of cases also; it was discussed during the recent Congress in Melbourne. The condensed discussion shows that considerable interest was taken in the point.[1] It may be recalled that the President of the Section of Medicine quoted the results in a series of 130 patients, of whom 59 had been examined by cardiac catheterization and 33 had been operated upon. Another series of interest has been published by O. H. Janton, R. P. Glover, T. J. E. O'Neill, J. E. Gregory and G. F. Froio, in which 100 consecutive cases of mitral stenosis are analysed.[2] The mortality rate fell in this series as greater experience was gained, and in all 78 patients were functionally improved. A considerable literature is now growing on the indications for and results of commissurotomy, but we need not here follow these authors' complete and critical analysis; we note, however, that they regard the presence of associated insufficiency of the mitral or the aortic valve as not rendering the patient unacceptable for operation unless there is more than minimal enlargement of the ventricle, or the electrocardiogram shows a left axis deviation. Of course, due notice must be taken of clinical information, and after even the most successful operation the patient must remain under careful survey. A further contribution to the subject has been made by Allan Wynn, M. B. Matthews, I. K. R. McMillan, and Raymond Dalley.[3] Their work has been on one important aspect alone: the estimation of the left auricular pressure both in normal subjects and in those suffering from mitral stenosis. Observations have been made on 37 patients before and after valvulotomy, and checked by others made on patients who underwent thoracotomy for pulmonary disease but had normal hearts. The chief object of this surgical and physiological research was to discover if gross mitral insufficiency could be detected when it was unrecognizable clinically, so as to select only the appropriate subjects for operation of the valve. Wynn *et alii* used an electromanometer with a direct writer, which recorded the pressure in the left auricle as delivered by a fine needle

[1] THE MEDICAL JOURNAL OF AUSTRALIA, October 11, 1952.
[2] *Circulation*, September, 1952.
[3] *The Lancet*, August 2, 1952.

inserted therein and attached to fine cardiac catheter tubing. The pericardium was opened only in the patients who were to be submitted to operation on the valve. Wynn and his colleagues studied the form of the pressure curve, and picture this in their article. They found that in mitral valve disease the form of the tracing resembled that found in the normal heart, but the pressure was higher. In all but one of a small number of patients who had mitral regurgitation as well as stenosis, no significance was noted in the left auricular pressure tracing; the same applied to those in whom mitral incompetence developed after valvulotomy. Thus this method does not provide a test which can be relied on to detect and assess degrees of incompetence. Still, the work and thought that lie behind the cautious movement of the surgeon's finger are helping us to obtain a better understanding even of so familiar a subject as mitral stenosis, and to make apt selection of that increasing class of patients who may benefit from this delicate procedure.

REVASCULARIZATION OF THE HEART BY A PEDICLE SKIN FLAP.

THE criticism has been made of certain American research centres that they are apt to publish material too early; in the words of a fellow countryman, they often "go off at half-cock". However, with a recent report on revascularization of the heart by a pedicle skin flap, presented by J. von Wedel *et alii*, of the department of surgery in the New York University Post-Graduate School,[1] a good case can be made out for early publication. The preliminary finding here is that in the experimental dog anastomoses can occur between the vessels of a skin pedicle and the vessels of the heart substance, and this is surely a significant discovery. In 25 dogs a thoraco-abdominal flap, based over the fifth and sixth ribs, was sutured to the surface of the heart. A segment of the sixth rib was removed to provide room for passage of the flap through the chest wall, "and the proximal portion of the flap was tubed so that the tubed part of the flap extended the entire distance between the chest wall and the heart". The distal open portion of the flap was then passed through an incision in the pericardium and sutured directly to the myocardium, approximately one-third of each ventricle being covered. Union was effected without any untoward results either of obvious cardiac embarrassment or of distorted electrocardiogram. The fact that macroscopic anastomoses had occurred was proved by several methods which will be accepted as convincing. It was found that if in the experimental animal the descending ramus of the left coronary artery was ligated no ill effects followed, the anastomotic circulation sufficing. Further experiments are promised to explore the possibility of the heart being protected against complete coronary occlusion. These will be awaited with interest.

OXYGEN BREATHING IN ANOXÆMIA.

A SPECIAL supplement to the *Acta medica Scandinavica* is devoted to a report on research on oxygen breathing in patients with lung and heart diseases and also in normal human beings subjected to experimental anoxæmia.[2] Particular emphasis is placed on pulmonary artery pressure, a circulatory feature demanding a special technique in its investigation and one which has been the subject of much recent research. In acute experimental anoxia in man oxygen administration reverses the circulatory changes induced, and one of these is that the increased pulmonary pressure falls to normal. In the chronic anoxia of patients with lung or heart diseases oxygen can give relief, but fails to make the circulatory changes normal. This indicates that oxygen therapy should be given at an early stage. Acute anoxia produces an increase in the work of the right ventricle, which oxygen administration rectifies. There is, both in normal subjects and in patients with lung diseases, a close correlation between systemic arterial oxygen saturation percentage and pulmonary artery mean pressure. A copious history of anoxæmia is given in this report, but it is evident that the fundamental work of Haldane and of Barcroft has not been adequately studied. Thus on page 24 there is a figure, redrawn from Barach, showing the dissociation curves of oxyhæmoglobin at two different partial pressures of carbon dioxide. This was demonstrated by Barcroft over forty years before Barach. Barcroft directed attention to the fact that in the active tissues there is a rise of temperature and also of carbon dioxide pressure, and both give a flattening of the curve; that is, they facilitate the liberation of oxygen from the hæmoglobin compound. The best portion of the article of 175 pages is that dealing with pulmonary artery pressure.

[1] *Science*, September 26, 1952.

[2] *Acta medica Scandinavica*, Supplement 269, accompanying Volume CXLIII, 1952.

CARDIO-VASCULAR DISEASE.

PART I of a recent *British Medical Bulletin* is devoted to cardio-vascular disease and maintains the high standard of this series.[1] The general practitioner will probably select first for reading the chapter entitled "The Natural History of Hypertension". Here the treatment is eminently sane, restrained and displaying the real scientific temper on the subject of essential hypertension, in which enthusiasm is often far ahead of judgement. The evidence for a vasomotor nervous abnormality or a circulating pressor substance is declared to be unconvincing. "It will seem that essential hypertension is due to an inherited peculiarity which may show itself as early as the second decade"; but what this peculiarity is eludes discovery so far. Probably the next article in general popularity will be that embodying the surgery of the heart, for here Brock in Britain in 1946 and Bailey in the same year in the United States of America introduced the surgical treatment of mitral stenosis in the face of much opposition from cardiologists. Sir Thomas Lewis in the very same year gave his opinion that such surgical treatment must fail because it was "based upon what, usually at all events, is an erroneous idea, namely that the valve is the chief source of trouble". What had happened was that the invention and subsequent continuous use of the stethoscope led to an exaggerated estimate of the physical features of valvular incompetence, and so the inevitable reaction took place and went too far in the other direction. The success of so many surgical attempts to alleviate the circulatory troubles of mitral stenosis has brought back the valve into prominence once more. What was denounced by White in 1944 as "ineffective and dangerous" and likely "to do more harm than good" is now a recognized and appreciated procedure. The dread that though stenosis might be relieved regurgitation might be aggravated has not proved well founded, for actually the release of the valve flaps usually leads to better closure in ventricular systole. Special mention might be made of Henry Barcroft's treatment of sympathetic innervation and denervation, Paul Wood's article on pulmonary hypertension, to which so much attention is being directed today, Sharpey-Schafer's discussion of peripheral circulation in circulatory failure, Aubrey Leathem's article on phonocardiography, in which it is pointed out that "the poor sensitivity of the human ear to the lower frequencies makes it easy for the phonocardiograph to record the low-pitched heart sounds better than they can be heard", the paper on the pathology of the coronary arteries and other equally important and attractive studies. Truly, as Professor McMichael remarks in his introduction, "of all the branches of medicine cardiovascular disease at the present day is the most richly endowed with the instruments of progress and the spectacular advent of surgery into cardiology has increased the demand for diagnostic application of the most advanced techniques as a preliminary to operation".

[1] *British Medical Bulletin*, Volume VIII, Number 4, 1952.

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Abstracts from Medical Literature.

RADIOLOGY.

Small Intestinal Rupture due to Non-Penetrating Abdominal Injury.

GEORGE JACOBSON AND RAY A. CARTER (*American Journal of Roentgenology*, July, 1951) report 19 cases of rupture of the small intestine due to non-penetrating injury of the abdomen and discuss the ætiological factors and clinical features. They state that retroperitoneal perforation of the duodenum was manifested by (*a*) outlining of the kidney by gas which also extended along the vertebral column and the crus of the diaphragm, (*b*) obliteration of the renal and psoas shadows by the retroperitoneal extravasation of duodenal content and (*c*) absence of positive radiological findings. Free subphrenic gas was demonstrated in only two cases of ruptured jejunum and in none of the ileum. Trapping of gas behind the transverse mesocolon may have been present in one case of ruptured jejunum. Small intestinal ileus of only a comparatively minor degree was visible in a majority of the patients in spite of the presence of generalized peritonitis in almost every case and a considerable lapse of time between the injury and the X-ray examination. The authors conclude that the great paucity of positive findings makes the X-ray examination of the abdomen of little value in excluding perforations of the small intestine following non-penetrating abdominal injuries.

Pulmonary Angiography in Bronchogenic Carcinoma.

DONALD J. SCHISSEL AND PHILLIP G. KEIL (*American Journal of Roentgenology*, January, 1952) have prepared pulmonary angiograms in 40 consecutive cases of bronchogenic carcinoma. In 37 cases characteristic changes were found in the blood vessel pattern of the involved lung. The most characteristic change was diminished vascularity within and distal to the carcinoma. Less frequent changes were obstruction or distortion of the superior *vena cava*, the pulmonary arteries or their branches. In 10 cases, representing one-fourth of the series, this vascular change was demonstrated in the presence of inconclusive findings from bronchoscopic examination and negative findings from microscopic study of bronchial secretions. The authors state that these results showed the importance of pulmonary angiography in diagnosis of lesions which are not readily available to diagnosis by bronchoscopy. They show further that the microscopic study of bronchial secretions is much more reliable when the lesion is within the reach of the bronchoscope, usually a location where biopsy is possible.

Inspissated Tuberculous Cavities.

M. B. HERMEL AND J. GERSHON-COHEN (*American Journal of Roentgenology*, January, 1952) discuss the mechanism whereby tuberculous cavities close. They state that obliteration of cavities occurs in two general ways: (i) By open healing, in which the cavity lumen remains patent. In this type the draining bronchus opens widely into the cavity lumen. The tuberculous components of the cavitary lesion are replaced by fibrous tissue. The lumen becomes epithelialized by either columnar or squamous epithelium. (ii) By closed healing, in which the lumen of the cavity either becomes obliterated by a scar or is replaced by retained caseation and inspissation. Healing by inspissation is the most frequent form. Inspissated cavities are quite stable in contrast to the intermittently blocking cavity or the balloon cavity; and provided no other active lesions are present in the lungs, a policy of judicious watchfulness is warranted. In establishing the diagnosis of an inspissated cavity, one should initially see a definite cavity. This cavity, when interval studies are carried out, should fill, and thus cast a shadow of increased density. The resultant opaque shadow should gradually shrink in size. Shrinkage of the lesion over the course of time is an important indicator of stability, since it denotes encapsulation by firm fibrosis. Only by means of serial X-ray examinations can the diagnosis be made. Without serial films, the differential diagnosis of a blocked cavity becomes the differential diagnosis of a rounded nodular lesion in the lung, and includes such entities as caseous parenchymatous foci, benign and malignant neoplasm, loculated effusions and cysts within the pulmonary parenchyma. A helpful finding in differentiating the inspissated cavity from the other entities is the "tennis racket" appearance of the tuberculous cavity. This appearance results from the reactive inflammatory change about the draining bronchus of the cavity, and it is almost always a concomitant finding in tuberculous cavities. The differentiation between the two types of cavities can be determined from the following criteria: the firmly inspissated cavity is associated with no evidence of systemic reaction, and it undergoes shrinkage over a period of time; the temporarily occluded cavity is associated with systemic toxæmia and either ballooning or failure of contraction of the cavity.

Synovioma.

ROBERT S. SHERMAN AND FLORENCE C. H. CHU (*American Journal of Roentgenology*, January, 1952) have made a radiological study of 32 histopathologically proved synoviomata. They state that synovioma occurs as a single tumour with almost invariably an intimate relationship to one of the joints. Upon gross examination it appears sharply circumscribed as if encapsulated. Often the tumour is firmly attached to adjacent tissues at one or more points, any one of which may represent either the site of origin of the tumour or an area of extension by invasion. The films did not always show whether the tumour was located entirely within or partially outside the capsular area, but it was always clear that the tumour mass as seen on the film was related to the capsule region in some degree; none was sufficiently far from a joint to permit one to say that there could be no contact with the capsule. The intimate relationship to the joint is an important point in X-ray diagnosis. The internal pattern of synovioma as revealed on the film was that of a homogeneous, structureless mass of water density. There were no dense areas suggesting septa, nor were there areas of relative radiolucence. The uniformity of the texture unbroken by any alteration seemed to be a rather constant feature and one considered useful in differential diagnosis from other soft tissue tumours. While the entire periphery of the lesion could rarely be seen, comparison of the different positions usually made it possible to reconstruct the general outline. When the edge was clearly demonstrated, it was seen to be regular and smooth. There was no peripheral line of increased density such as might be cast by a denser capsule. For the most part, there was little or no evidence of infiltration into neighbouring structures except for the few cases in which contiguous bone involvement took place. Calcification within the tumours and bone destruction were uncommon findings. The authors conclude that all clinically recognizable synoviomata should be identified on the skiagram, and that often the radiologist may be able to suggest the diagnosis of this tumour.

"Telepaque": A New Cholecystographic Medium.

WILLIAM H. SHEHADI (*American Journal of Roentgenology*, September, 1952) states that "Telepaque" (3-(3 amino-2,4,6-triiodophenyl)-2-ethylpropanoic acid) is a new compound which seems to satisfy the requirements of an ideal cholecystographic medium better than any of the media now used for cholecystography, and for that reason is considered superior. From observations made on a non-selected series of 310 cases, "Telepaque" presents the following features: (i) a decidedly low level of side reactions; (ii) ready and rapid absorption, prompt response of the gall-bladder to a fat meal, and rapid elimination from the system; (iii) greater density and improved visualization of the gall-bladder; (iv) frequent visualization of the bile ducts. This introduces a new field in the study of the biliary tract. At this time the recommended dose is six tablets (three grammes), to be given ten to twelve hours before the scheduled examination. For very obese patients a twelve tablet (six grammes) dose may be indicated.

The Klippel-Feil Syndrome.

MELVIN SHOUL AND MAX RITVO (*American Journal of Roentgenology*, September, 1952) state that the "Klippel-Feil syndrome" is a condition characterized by specific anomalies of the cervical vertebræ. The lesion comprises primarily fusion of two or more cervical vertebræ and manifests itself clinically by shortening and limitation of mobility of the neck. Associated with these malformations are often anomalies of other segments of the spine, congenital abnormalities of other portions of the skeleton and neurological disturbances. If the vertebral coalescence is slight in degree and other associated spinal anomalies are absent, the condition may produce no clinical manifestations and go unrecognized unless radiological studies are performed. In the more severe cases

the clinical picture is characteristic and the diagnosis can often be established by inspection alone. The neck is much foreshortened or entirely absent. The head is sunken and implanted on the chest. The hair line posteriorly is very low, extending to the upper limit of the thorax. The head is often in a position of torticollis. Less common manifestations are facial asymmetry, mirror movements, difficulty in breathing and swallowing, and shortness of breath. Movement of the head is usually limited, but motion causes no pain. The ætiology is unknown. There is a disorder of the mesodermal and ectodermal tissues, and the deformities apparently commence during the third to the eighth week of development of the fœtus. The disease is compatible with long life, although associated congenital anomalies, which often occur, result in an altered prognosis. The subject is very susceptible to fracture of the cervical vertebræ with relatively slight trauma, owing to the limited or absent mobility of the neck, and must avoid violent exercise and trauma to the head and neck. X-ray examination is essential to establish the diagnosis and to determine the character and extent of the malformations in the cervical part of the spine as well as other skeletal anomalies. Two or more central vertebral masses are solidly united into a single bony mass with complete absence of the intervertebral spaces and disks. The lateral masses are irregular or fused, and the spinous processes are small, deficient or bifid. The intervertebral foramina are smooth in contour, but are frequently smaller than normal and oval rather than circular in shape. Fusion of the atlas and occiput is common. Anomalies of the more caudal portions of the spine—anterior and posterior *spina bifida*, sacralization of the last lumbar vertebra and hemivertebræ—may be found. Scoliosis and kyphosis are occasionally present. Radiological studies of the skull are indicated, to demonstrate associated deformities, such as platybasia and coarctation, asymmetry and other malformations of the *foramen magnum*. Sprengel's deformity, or congenital elevation of the scapula, and cervical ribs are often present, their extent varying considerably on the two sides. The apices of the lungs are raised. The technical aspects of the X-ray examination are important to demonstrate the character and extent of the changes. Because of the short neck and sunken head, skiagrams of perfect detail are difficult to obtain, particularly with the antero-posterior and oblique projections, as the occiput and mandible overlie and obscure the cervical vertebræ. Skiagrams with the jaw in rapid motion may be helpful with antero-posterior films. Laminagraphy may be essential if the cervical vertebræ are much coalesced.

Transverse Tomography of the Thorax.

Q. DE VULPIAN *et alii* (*Revue de la tuberculose*, 1952, Number 6) describe a method of transverse tomography of the thorax and the results of its application. It is admitted that technical improvements will be necessary in order that the method may be of value in the diagnosis of pleural, mediastinal and pulmonary diseases.

PHYSICAL THERAPY.

The Sieve in Radiotherapy.

B. JOLLES (*The British Journal of Radiology*, August, 1952) gives a progress report on the sieve method (sometimes called the grid method) in deep X-ray therapy. He discusses the technique, its rationale and biological implications, and briefly surveys the physical aspects. He states that he used the sieve technique in patients with malignant disease between 1941 and 1945; then elaboration of the technique followed, and by the end of 1951, a total of 54 patients had been treated. The principle of the method is that through a lead chess-board sieve, with 0·5 to 1·5 centimetre squares, portions of the tumour are exposed to radiation while other portions of similar area are protected in order that important structures remain undamaged and can take part in repair. With superficial tumours, after a substantial proportion of the total dose has been given, another lead sieve is used in which the order of opaque and transparent areas is reversed. Exactness is essential in every detail of the technique. Lead rubber is no longer used, having been discarded in favour of sheet lead. Dental wax, plaster of Paris or other material is used to make a mould to hold the sieve in position. Circles can be used for the sieve apertures, but squares of 0·5 to 1·0 centimetre are preferred because a complementary sieve is easier to make with them. The X-ray applicator is directed vertically on to the sieve, and irradiation is given daily, generally 500*r* daily. Doses of up to 10,000*r* in three weeks have been given in some cases. There is no doubt regarding the increased skin tolerance to doses following the sieve method as compared with conventional X-ray therapy. The method has been found useful in difficult cases of superficial epithelioma, which can be successfully treated without risk of necrosis, and for palliative treatment of deep-seated tumours, such as carcinoma of the uterus, the lung and the bowel. The curative value of the method in such cases has still to be assessed. The physical aspects of the method are briefly discussed.

"Radiocurability" of Cancer.

MAURICE LENZ (*The American Journal of Roentgenology, Radium Therapy and Nuclear Medicine*, March, 1952) discusses the "radiocurability" of cancer (by which he means freedom from clinical evidence of cancer for at least five years after treatment) and the factors which influence it. These factors include the natural clinical course of the untreated cancer, its location, extent and accessibility, its radiosensitivity and the patient's tolerance of the required dosage. The author states that an inherent tendency to slow growth will increase the proportion of five-year survivors among treated patients. A location where symptoms are prominent and where the part is accessible to clinical examination facilitates early diagnosis and treatment. Estimates of the extent of cancer based on microscopic examination are more reliable than clinical impression. Thus in mammary cancer, the axillary nodes may be shown microscopically to be extensively involved when this is not realized clinically. "Radiocurability" is reduced with increasing extent of the cancer. Thus the five-year survival rate after deep X-ray therapy among 242 patients with lymphosarcoma irradiated at the Presbyterian Hospital, New York, decreased from 54% of 37 cases with one site clinically involved to 9% of 135 cases with three clinically recognizable sites. The inherent radiosensitivity of the growth determines the tumour dose required for its destruction. Improvement in radiocurability was noted with increase in tumour doses in the treatment of cancer of the bladder, larynx and breast and lymphosarcoma. It is suggested that tumour doses of 5000*r* in five to six weeks are necessary for lymphosarcoma of the nose and throat to ensure permanent disappearance. For most malignant growths, high doses are required. The author discusses the tolerance of the normal tissues and how it is affected by the time factor, the size of the irradiated field or volume, the type of radiation, poor blood supply or added infection. He states that intensive irradiation is not tolerated by infected inflamed tissues. Infection should, if possible, be cleared up before irradiation is given. The value of the irradiation physicist as a member of the radiotherapeutic staff of a hospital is stressed, and for accurate modern work his presence is essential. He makes a plea for improvement in the training of radiotherapists in the United States and the separation of radiotherapy as a distinct specialty from diagnostic radiology, a state of affairs which has existed in England and Scandinavia for some years.

Artificial Radioactive Sources for Interstitial Therapy.

W. K. SINCLAIR (*The British Journal of Radiology*, August, 1952) states that in some sites in the body where the interstitial implantation of radon seeds or radium needles has been used, it would be preferable to have sources more flexible than those available with the natural isotopes. Artificial radioactive isotopes, particularly Co^{60} and Ta^{182}, have been suggested as alternatives to radium, and Au^{198} as alternative to radon. Tantalum (Ta^{182}) wire as a substitute for radium, and radioactive gold (Au^{198}) grains as a radon seed substitute are described. Tantalum (Ta^{182}) has a long half-life of 111 days, is well tolerated by the tissues and is preferable to cobalt for interstitial purposes. Tantalum wire sheathed in platinum with a total diameter of 0·4 millimetre has been prepared and possesses sufficient flexibility to be very easily bent, but is rigid enough to retain its shape. The platinum sheath absorbs all the β radiation from the tantalum. This wire has been used in the treatment of carcinoma of the bladder. Radioactive gold (Au^{198}) has a half-life of 2·72 days, and gold grains encased in platinum have been used as an alternative to radon seeds, and implanted by means of a new type of gun. The grains produce approximately the same reaction as radon seeds, but the handling procedure is simple, and the method of introduction is more simple than with radon seeds.

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Special Articles for the Clinician.

(CONTRIBUTED BY REQUEST.)

XLVI.

THE BLOOD SEDIMENTATION RATE.

THE blood sedimentation rate may be defined as the rate at which red blood corpuscles settle or form sediment when a measured amount of blood, to which an anticoagulant has been added, is placed in a standard glass tube. The tube is graduated from the top in millimetres. Various anticoagulants are used, and it is advised that an observer should use the same amount of the same anticoagulant in every test.

The Westergren and Wintrope methods are in common use.

In the Westergren method 3·8% sodium citrate solution is used; 0·4 millilitre of the solution is drawn into a syringe, and blood from a vein is drawn up to the 2·0 millilitre mark.

Wintrobe uses a hæmatocrit; he takes 5·0 millilitres of blood and places it in a vessel containing 4·0 milligrammes of solid potassium oxalate and 6·0 milligrammes of solid ammonium oxalate.

After estimation of the blood sedimentation rate, the hæmatocrit may be centrifuged, and the volume of packed leucocytes and platelets and the icteric index can be measured. Heparin is used by some as the anticoagulant.

The test is delicate, and so it is important that attention be paid to numerous details when the test is being carried out. All apparatus must be perfectly clean. The tube must be vertical throughout the test, as any departure from this causes an increase in the rate.

Some observers advise that the test should be carried out within two hours of taking the blood, and others say within three hours; so it may be assumed that three hours is the maximum time. Probably two hours is better.

In view of the need for great care in the performance of the test, it is desirable that anyone not familiar with the technique should learn it in a laboratory where it is a routine.

There are two methods of making readings. In the first the time required for the upper level of sedimenting corpuscles to fall a specified distance is recorded. In the second the distance the corpuscles have fallen in a fixed time, usually one hour, is read. The second is the more popular and is used in the Westergren method.

Some observers take readings in one hour and two hours. Readings every five minutes have been suggested, but such a tedious method would be an unwarranted waste of time, unless very distinct advantages could be proved.

The sedimentation rate is greater in women than in men, and it is remarkably constant in normal people.

Westergren gives the normal rate for men as 3·0 to 5·0 millimetres in one hour and 7·0 to 15·0 millimetres in two hours; and for women, 7·0 millimetres in one hour and 12·0 to 17·0 millimetres in two hours.

Wintrobe gives the normal rate for men as 0 to 6·5 millimetres in one hour, in 86% of 137 men, the average being 3·7 millimetres; and for women as 0 to 15·0 millimetres in one hour, in 88% of 100 women, the average being 9·0 millimetres.

Although the test has been in use for many years, many of the factors concerned are still unknown.

Apart from possible technical errors, certain disturbing elements are known. Among these are increases in the blood content of fibrinogen, cholesterol and globulin, which increase the rate, and of albumin, nucleoprotein and lecithin, which reduce it.

The rate is increased as a rule in association with severe anæmia, but with chronic anæmia there may be little alteration. Charts have been drawn up to correct the errors due to anæmia, but although these are useful, none is entirely reliable. This is because they tend to over-correct the error.

If the corrected rate is above normal, there is an organic lesion. The blood sedimentation rate is usually increased during the menses, and in order to obtain accurate results, blood should not be taken during, and for a day or two before and after, a menstrual period.

During pregnancy, the rate is raised from the fourth month and does not return to normal until three or four weeks after parturition. It may reach a height which suggests that a pathological condition is present.

The increase in rate during pregnancy may cause some difficulty if abortion occurs, for it may be simply related to the pregnancy, or it may be due to some other cause such as retention of membranes; if infection is present, the rate is likely to be much increased.

Apart from the exceptions mentioned and possibly some others, the rate is normal in healthy subjects.

The destruction of tissue cells in infections and toxic conditions is the most important cause of an increased blood sedimentation rate.

The test is non-specific and is comparable with the temperature and pulse rate in giving information of a general character. The rate may be increased when temperature and pulse rate are normal.

In acute general infections it is increased, but in localized acute inflammation it varies with the nature and severity of the infection. In a mild and local infection, such as a dental abscess, it may be normal. It may be normal in acute catarrhal conditions, but, as a rule, a normal rate may be taken to indicate good health. In general it is a measure of the presence and intensity of a morbid process.

Estimation of the blood sedimentation rate may be of value in diagnosis and prognosis.

Since it is not a specific test, it is only one link in the chain of evidence on which a diagnosis is made, and it is often of little importance. Sometimes it is included in a list of investigations drawn up when a patient comes under observation, and the patient has an additional needle puncture which other observations may show to have been unnecessary.

It may be very valuable when other investigations have failed to provide a diagnosis, as an unexpected high reading will lead to a review of the history and clinical findings and to the adoption of other forms of investigation which may lead to a correct diagnosis.

An increased rate is usually reliable.

When there is evidence of the presence of organic disease, a normal rate may be misleading, but there are organic conditions in which the rate is not increased.

Estimation of the sedimentation rate may be valuable when a decision has to be made on whether there is organic disease. It may be normal in carcinoma of the liver. In malignant disease it may be high even if the blood has been kept for twenty-four hours before the estimation is made.

A high rate (corrected) in patients under treatment for pernicious anæmia has led to a diagnosis of carcinoma of the stomach or the presence of a focus of infection; so it is desirable to perform the test in cases of pernicious anæmia when progress is not as expected.

It is said to be of value in the early diagnosis of infective hepatitis, and especially in its differentiation from clinical malaria. In the former the rate is less than 10·0 millimetres and in the latter it is more than 10·0 millimetres.

Probably the blood sedimentation rate is of most value in prognosis, and as an indication of progress and of the effect of treatment. Here reference may be made to anomalies which have been reported during the last year.

Gilmour and Sykes (1951) found the Wintrobe method misleading in a few important cases. In a fairly large series of cases a raised Wintrobe figure was always accompanied by a raised Westergren figure; but a raised Westergren figure was not accompanied by a raised Wintrobe figure in as many as 27% of the female and 28% of the male cases. They conclude that the Westergren is more sensitive and more reliable than the Wintrobe method.

Goldberg, Glynn and Bywaters (1952) reported somewhat similar findings, and thought that the Westergren rate was a better index of the clinical state. They were dealing with rheumatic conditions. The anomaly was found in 10 out of 86 cases.

Gilmour and Sykes offered no opinion on the mechanism leading to the anomaly, but Goldberg *et alii* were making investigations and suggested that it probably depended on the anticoagulant's effect upon the pH.

In tuberculosis, estimations of the blood sedimentation rate may be of great value, but they are not diagnostic; the rate may be normal when *Mycobacterium tuberculosis* is present in the sputum, and it may be raised in tuberculous patients with some non-tuberculous condition, such as an

intercurrent infection, which may be responsible for the increased rate.

The test is a useful guide to progress and may be used as an indication for treatment. The rate being related directly to the number of red blood corpuscles, red cell counts must be made and the blood sedimentation rate adjusted accordingly. Digestion, exercise, menstruation and other conditions affect the rate; so the test is open to many fallacies. However, when a patient is undergoing a course of treatment, a steady improvement in the rate is helpful. A steady deterioration in the rate increase should lead to reconsideration of the treatment. A sudden unexpected rise or fall may suggest some anomaly, and a repetition of the test is indicated.

In patients under treatment with artificial pneumothorax, or after a thoracoplasty, the test may show that all is not well before changes in X-ray films are apparent.

In acute pulmonary tuberculosis with pneumonic spread it is much increased and may be of value if improvement occurs. In general it is an index of the severity of the infection.

In chronic tuberculosis it is of greater value, as it increases when the disease is active and decreases when the process becomes stationary or healing occurs.

Recrudescence may be shown by an increased rate before evidence of this appears in the form of an increase in physical signs.

In other forms of tuberculosis, estimations of the blood sedimentation rate may be used in the same way.

It is essential, of course, that repeated estimations of the rate be made when it is used for the purposes referred to in this disease. Leprosy, also due to an acid-fast bacillus, may be mentioned here, because estimations of the blood sedimentation rate are said to be of value in estimating progress during treatment.

The blood sedimentation rate is raised in acute rheumatism, but this is of little importance, during the early pyrexial period, in comparison with the value of repeated estimations during the later stages, and during convalescence, when a gradual decrease in the rate is expected. It is then a valuable indication of the subsidence of the infection, and it may be helpful when a decision is being made about allowing a patient to become more active. Much the same applies in rheumatic carditis, in which a normal sedimentation rate gives evidence of inactivity. As stated in reference to other conditions, there must be absence of other evidence of cessation of activity as well as the normal sedimentation rate.

In children, a micro method of estimating the blood sedimentation rate may be used.

In cardiac affections the blood sedimentation rate is increased in some and decreased in others. It is decreased in congestive cardiac failure and in congenital heart disease with cyanosis. It is increased in the early stages of acute cardiac infarction, and is said to be of help in diagnosis when an electrocardiogram is not available, but with the widespread availability of the electrocardiograph, it must be unusual for the blood sedimentation to be used often for diagnosis.

In infective endocarditis the rate is increased and, as in other infections, serial estimations may be useful evidence of the subsidence of the infection, but here again the clinical condition of the patient must be considered as well.

The rate is likely to be raised in the presence of malignant tumours of the brain and in various inflammatory conditions, in tuberculoma and in subdural hæmatoma.

It is said to be normal in acute appendicitis in the first twenty-four hours and may help in differentiating this from other inflammatory conditions in the abdomen in which the rate is raised.

The rate is increased in carcinoma of the stomach, and in peptic ulcer it is normal or only slightly increased unless the ulcer is large or penetrating and associated with perigastric inflammation.

It seems that the blood sedimentation rate is of limited value in many of these conditions and that other methods of investigation are of much greater importance.

In infective arthritis, acute gout and active rheumatoid arthritis the rate is increased, and in osteoarthritis it is normal or only slightly raised. Of these conditions, estimation of the blood sedimentation rate is likely to be of most value in rheumatoid arthritis. It may be helpful in diagnosis and as a control in some forms of treatment. Forestier thought that those patients in whom the rate was exceptionally high reacted best to gold therapy. It is also a valuable means of recognizing abatement in the activity of the disease. It may be used also in the control of vaccine therapy.

Reference has been made to many conditions in which an increased blood sedimentation rate may be found, but no attempt has been made to include all.

While an increased rate is usually of more value, a normal or decreased rate may be of value sometimes.

Again it may be said that while this estimation may be useful in diagnosis, prognosis and treatment, it is not of value alone, and must be considered with symptoms and signs and with all investigations and observations which are available for the solution of difficult problems.

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British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held on June 18, 1952, at the Royal Alexandra Hospital for Children, Sydney. The meeting took the form of a series of clinical demonstrations by members of the honorary medical and surgical staff of the hospital. Parts of this report appeared in the issues of December 6 and 20, 1952.

Congenital Cystic Disease of the Lung.

DR. T. Y. NELSON showed a female child, aged twelve months, who had been first admitted to hospital in July, 1951, at the age of three months. For four days she had had a moist cough, dyspnœa and attacks of cyanosis.

On examination, the patient was seen to be well nourished and of good colour. Her temperature was 102° F. and respirations were rapid. Examination of the chest revealed hyperresonance and diminished air entry on the right side, and crepitations at the base of the right lung. X-ray examination revealed pronounced over-distension of the right lung, with gross emphysema and probably some cysts; no air could be seen in the pleural cavity. Further films were requested, to elucidate the ætiology.

Oxygen was given by intranasal catheter, penicillin was given in doses of 50,000 units every six hours, and "Coramine" was given as required. The child's temperature fell rapidly after two injections of penicillin, and the dyspnœa subsided over twenty-four hours. The administration of penicillin was suspended after one week. A further X-ray examination revealed an advanced degree of cystic disease of the right lung, which was thought to be congenital in origin. The heart and mediastinum were considerably displaced to the left. The child was discharged from hospital after two weeks, to be readmitted later for operation.

On April 14, 1952, the child was readmitted to hospital after a further respiratory infection, for which she had been in a country hospital for three weeks. In preparation for operation her blood group and Rh status were determined and cross-typing was carried out, and she was given orally 25 milligrammes of chloramphenicol per kilogram of body weight. Anæsthesia was by ether ("open" method), intubation, nitrous oxide and oxygen, cyclopropane and "Tubarine". The sixth rib was resected and the fifth rib divided, and the chest was opened along the sixth rib bed. A large cyst presented in the wound; it involved the lower lobe of the right lung, and this lobe occupied most of the right side of the chest. The right lung was rotated about its hilum, so that the middle lobe, which also contained a small cyst, was lying in the upper part of the left hemithorax. The upper lobe of the right lung was lying across the heart so that it came to lie mainly in the left side of the chest. The mediastinum was absent. The left lung was in a collapsed condition and looked agenetic. A right lower lobectomy was performed and the wound was closed without drainage.

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Oxygen was given for a few hours after operation through a nasal catheter, and a transfusion of about 600 millilitres of blood was given. Penicillin was administered for ten days. By the second day the trachea was felt in the midline and chest expansion was symmetrical. A slight collection of fluid at the base of the right lung resolved in ten days, and the child was perfectly well when discharged from hospital three weeks after operation. Histological examination of the resected lung confirmed the diagnosis of congenital cystic disease. A follow-up X-ray examination revealed reexpansion of the upper and middle lobes of the right lung and of the left lung, and restoration of the mediastinum.

Dr. Nelson said that the cyst was under a considerable degree of tension, and it was questionable whether the left lung had ever expanded. At any rate it had been deflated and compressed since the initial attack at the age of three months, and yet a few days after operation the left lung was fully expanded. After the initial attack of cyanosis and dyspnœa the child had not been embarrassed by the cyst, but in view of the gross displacement it was thought that removal was imperative. Examination of the specimen showed its multiocular character; the wall was lined by bronchial epithelium and contained a fair amount of muscular tissue, which pointed to the congenital nature of the condition.

Pneumonectomy for Bronchiectasis.

Dr. Nelson's next patient was a girl, aged eight and a half years. She had had her tonsils and adenoids removed at the age of eighteen months for recurrent nose and ear infections. At the age of two years she developed a cough with copious purulent sputum, and the amount of sputum gradually increased. Postural drainage and breathing exercises were commenced, with the prophylactic administration of sulphathiazole. At the age of three and a half years the child underwent bilateral antral lavage and bronchoscopic suction. At the age of four years she again underwent bilateral antral lavage, and a bronchogram was taken which showed a normal left lung and some cylindrical bronchiectasis in the lower lobe of the right lung. At the age of five years (1948) a further bronchographic examination revealed atelectasis of the lower lobe of the left lung, causing crowding of bronchi in that area. After the examination the child developed respiratory stridor, and further suction was carried out.

On February 26, 1951, at the age of seven and a half years, the child had a further bronchoscopic examination, and copious mucopus was present on both sides. On March 19 a bronchographic examination revealed bronchiectasis in all the lower lobe of the left lung and lingular bronchi, and some in the right retrocardiac branch.

On August 4, 1951, the child was admitted to hospital for lobectomy. "Pentothal", nitrous oxide and oxygen were the anæsthetic agents used, with the addition of "Tubarine"; an endotracheal tube was passed and controlled respiration was used. Left thoracotomy with resection of the seventh left rib was carried out, numerous adhesions from the lower lobe of the left lung to the diaphragm were divided, with considerable bleeding, left lower lobectomy and lingulectomy were performed, and the wound was closed with drainage of the pleural cavity. After operation there was very little drainage from the tube. Considerable amounts of air and fluid were seen in an X-ray film of the chest on the first day after operation; this condition persisted for one week. Bronchoscopic suction was performed on the second day after operation. One month after operation an opaque area was seen in the left pleura in two skiagrams, and was thought to be due to either fluid or pleural thickening; it was still present when the child, otherwise well, was discharged from hospital one month later.

On February 11, 1952, the mother thought that the child's condition was worse than before operation, and she had failed to regain weight. Accordingly she was readmitted to hospital for decortication of the upper lobe of the left lung. At the second operation, which was undertaken because of failure of the upper lobe to expand, it was found that the bronchus to the upper lobe was compressed by large glands on either side joined by strong bands of fibrous tissue. It was not possible to inflate the lobe, and there was no inflammatory exudate on the surface to prevent it. The condition was a post-operative reaction, as the glands had not been present at the first operation. Even after their removal it was not possible to inflate the lung by positive pressure, and lobectomy was performed. Examination of the specimens revealed a condition of cylindrical bronchiectasis of the lower lobe and lingula, and examination of the upper lobe removed at the second operation also revealed a condition of bronchiectasis which had developed since the first operation; the findings demonstrated the importance of achieving early expansion in the post-operative period. The subsequent course had been satisfactory.

Ectopia Vesicæ.

DR. J. STEIGRAD showed a male child, aged one and a half years, who had been first admitted to the hospital on December 1, 1950, at the age of one day, with obvious *ectopia vesicæ*. The posterior bladder wall bulged noticeably when the child cried. At the upper end the bladder wall was connected with a large fleshy umbilical cord. At the lower end there was a small epispadic penis, leading back from which the penile urethra could be seen. Bilateral inguinal herniæ were also present. No other abnormalities were detected. X-ray examination revealed a large gap at the *symphysis pubis*. The baby was discharged from hospital on January 10, 1951, unrelieved.

The child was readmitted to hospital on June 6, 1951, at the age of six months. Pre-operative treatment consisted of chemotherapy and the administration of antibiotics and bowel washouts. At operation on June 14 the right ureter was immobilized and implanted into the sigmoid colon. The child's post-operative condition was good, and on July 5 the other ureter was transplanted into the sigmoid colon. After an uneventful convalescence the patient was discharged from hospital on July 7.

On November 28 the child was again readmitted to hospital; at that time he was gaining some control of his bowel. On December 6, after pre-operative blood transfusion and chemotherapy, the ectopic bladder was excised and the abdomen was closed. The child was discharged from hospital on February 3, 1952. Pathological examination of the bladder revealed hypertrophy with metaplasia of the surface epithelium and chronic inflammation of the extroverted viscus.

Dr. Steigrad's next patient was a boy, aged six years, who had been first admitted to hospital on February 26, 1949, at the age of two and a half years, with *ectopia vesicæ*. There was no history of past illnesses and nothing relevant in the family history. On examination of the child, the posterior surface of the bladder was ectopically placed in the abdominal wall just above the symphysis. Both ureters were low and in a fold of skin. There was some epithelialization of the bladder wall, but the bladder was still tender to touch. The penis was just below the bladder. Examination of other systems revealed no abnormality. After pre-operative treatment by saline bowel lavage and the administration of streptomycin, penicillin, sulphonamide and blood transfusion, operation was undertaken on February 24. The right ureter was mobilized and divided and then implanted into the sigmoid colon. Post-operative vomiting necessitated the intravenous administration of fluid; otherwise convalescence was uneventful. At a further operation on March 21 the left ureter was mobilized and implanted into the sigmoid colon. Recovery was uneventful, and the child was discharged from hospital on April 3. During his stay in hospital, blood examination on four occasions between February 16 and March 31 showed the hæmoglobin values to be 10·5, 13·5, 11·7 and 12·0 grammes *per centum* respectively. On February 16 an X-ray examination of the pelvis revealed wide separation in the neighbourhood of the *symphysis pubis*, apparently due to failure of bony development of the upper pubic rami.

The child was readmitted to hospital on September 4, 1949. On examination of the patient the bladder wall was evident just above the base of the penis, and he was passing fæces and urine into the bed. No other abnormality was detected. At operation on September 8 the ectopic bladder and epispadias were evident. There was a dense arcuate band from one pubic bone to another and a small meatus between divaricating recti. A curved incision was made around the ectopic bladder with its apex at the top. The bladder was raised from the underlying peritoneum and excised, the peritoneal cavity not being opened. The central strip of bladder mucosa, hinged below, was returned and secured to the freshened splayed urethra. The ventral prepuce was incised below the corona, and the foreskin was opened out, perforated and threaded over the glans and then sewn over the mucosal flap. The abdomen was closed. The child was discharged from hospital on October 17. Pathological examination of the excised bladder showed it to be covered in part by metaplastic epithelium and in part by ectopic epithelium of alimentary type.

The child was once more admitted to hospital on May 10, 1950. There were some adhesions around the base of the penis and some raw unhealed edges. At operation on May 11

the raw edges were freshened and the adhesions divided. The child was discharged from hospital on May 27.

On November 15, 1950, once again the child was admitted to hospital. A small rudimentary penis was present. At its base there were two communicating tracts of mucous membrane between its surface and the underlying bladder remnant. Fairly pronounced epispadias was present. At operation on November 16 the edges were freshened, the urethra was reconstituted and the surface of the glans was closed. The child was discharged from hospital on November 27.

The child was finally admitted to hospital on September 17, 1951, because of nocturnal enuresis. The penis was rudimentary, with a large sinus on the right side of the base and a smaller sinus on the left side. Excretion pyelography on September 20 revealed mild to moderate dilatation of the upper half of the right ureter, renal pelvis and calyces, but no calculus. The renal shadows were not enlarged, and excretion of dye was satisfactory on both sides. There was considerable widening of the *symphysis pubis*. At operation on September 20 the fistulæ were closed and the penis was repaired. Dorsal and ventral flaps were made and then sutured so as to reconstitute the glans. The child was discharged from hospital on October 2, and had not been in hospital since.

Dr. Steigrad also showed a male child, aged two years, who had been admitted to hospital on November 11, 1951, when eighteen months old with obvious *ectopia vesicæ*. He had first been examined at the Royal Newcastle Hospital when two weeks old, and prior to his admission was treated for rectal prolapse, having had an operation in December, 1950; but the prolapse had recurred several times.

On examination of the child, an area of the abdominal wall was lacking, through which could be seen bladder wall. The penis was just below the hiatus, and the scrotum below that. There was a right inguinal hernia. The other systems were clear. Pre-operative treatment with chemotherapy and bowel washouts was given, and the child was operated on, on November 29. The right ureter was mobilized and transplanted into the sigmoid colon. Convalescence was uneventful, and on December 20 a second operation was performed. Through the previous scar the abdomen was opened, and a left uretero-sigmoidostomy performed. The child was given a blood transfusion after this operation, and after an uneventful convalescence was discharged from hospital on January 15, 1952.

He was readmitted to hospital on February 21 because of the hernia which was coming down more frequently, and was becoming more difficult to replace. On examination of the patient, the *ectopia vesicæ* and epispadias were as before. The hernia was larger than on his previous admission. Both testes were in the scrotum. After the usual pre-operative treatment the child was operated on, on February 28. The bladder was excised, and the epispadias was repaired by Ombredain's method. A bilateral inguinal herniorrhaphy was performed, and the suprapubic wound was closed with drainage. The wound was slow in healing, but the child was discharged from hospital on March 30.

Exomphalos.

Dr. Steigrad's next patient was a girl, aged one year, who had been admitted to hospital on May 18, 1951, when one day old, from the Women's Hospital, Crown Street, Sydney. She was the third child of the family, the first daughter having been born with a small umbilical hernia. The pregnancy had been normal, the baby being born two weeks prematurely.

On examination of the child, severe exomphalos was present, there being a large number of coils of small bowel extruding, with some large bowel and stomach. There were no other developmental abnormalities, and the other systems were clear. At operation on May 18 no sac was found, and the opening in the abdominal wall was to the right of the umbilical cord. The hiatus was enlarged downwards, the stomach and intestines were returned to the peritoneal cavity, the rectus sheath was returned together and the skin was closed. Continuous gastric suction and the intravenous administration of fluids were commenced and continued for three days. Meconium was passed three days after operation. There was some œdema of the lower abdominal wall and the vulva. Chemotherapy was commenced immediately after operation and continued for a week. Gradually the baby was transferred to oral feedings, and then breast feeding was established and the baby was discharged from hospital on June 8.

Dr. Steigrad then showed a baby, aged eight months, who had been admitted to hospital on October 1, 1951, after a normal delivery on the same day, with an exomphalos the size of a tennis ball, completely covered. No other abnormality was detected.

At operation on October 1 the exomphalos contained small bowel, liver and stomach. A peripheral circular incision was made in the skin around the sac, the cord vessels were tied and the cord was excised. The skin flaps were widely undermined and the edges approximated over the sac. No attempt was made to return the sac contents into the abdomen. Recovery was uneventful, and the child was discharged from hospital on October 19. A photograph was taken before discharge. Follow-up examination showed that the hernia was becoming smaller. An attempt was to be made to repair the abdominal wall.

Protruding Ears.

Dr. Steigrad's next patient was a boy, aged seven years, who had been admitted to hospital on May 28, 1952, because of protruding ears since birth. The left ear was worse than the right. A photograph was taken prior to operation. At operation on May 29 posterior incisions were made and elipses of cartilage and skin were excised. The skin edges were then apposed. Recovery was uneventful, and he was discharged from hospital on June 7.

Dr. Steigrad also showed a male child, aged ten years, who had been admitted to hospital on April 25, 1951. He had had protruding ears since birth, the left being worse than the right. A photograph was taken prior to operation. At operation on April 26 posterior incisions were made, elipses of cartilage were excised from each ear, and skin was excised along the line of the antihelix. The skin was then closed, and pressure dressings were applied. Recovery was uneventful, and the child was discharged from hospital on May 10.

Cervical Thymic Hyperplasia.

Dr. Steigrad next showed a male patient, aged four years, who had been admitted to hospital on April 9, 1952. He had lived in Australia for one year, having previously resided in northern Italy. There was no history of tuberculosis in the family. A lump had been noticed in his neck since October, 1951. It became almost as big as a hen's egg, but on his admission to hospital it was hardly visible. There was no history of discharge and he was symptomless.

On examination of the patient, deep to the right sterno-mastoid there was a stony hard tumour about one inch long by half an inch. It was smooth and mobile up and down. There was a palpable right cervical gland. A firm rather similar tumour was palpable on the left side. No other abnormalities were detected. A full blood count on April 17 gave the following information. The erythrocytes numbered 4,800,000 per cubic millimetre, the hæmoglobin value was 12·0 grammes *per centum* and the colour index was 0·82. The cells varied in size from normal to microcytic, but the majority were normal; their shape and colour were normal. The leucocytes numbered 19,900 per cubic millimetre, 52% being neutrophile cells, 42% lymphocytes, 4% monocytes, and 2% eosinophile cells. X-ray examination of the chest revealed no abnormality.

At operation on April 10, beneath the right sterno-mastoid in a fibrous sheath a tumour running vertically was found. It extended above the level of the thyroid cartilage, and downwards towards the mid-line behind the sternum. The tumour was dissected down to the sternum, but as the lower end could not be seen it was ligated and cut there. It was attached to the sheath of the carotid artery. The skin was closed. A smear from the tumour was examined and culture was attempted, but no acid-fast bacilli were seen. A pathological examination was carried out. The entire specimen weighed 13 grammes; it was an elongated tube of firm nodular tissue of pale brown colour. Examination of the incised portion revealed a small central space lined by deep yellow, firm and adherent granular material. Sections were taken at the proximal end and at various levels distal to it. Microscopic examination of the sections revealed that at all levels the tube was composed of thymic tissue with a clear demarcation into cortex and medulla. The Hassal's corpuscles were large and many were degenerated, while the thymic lymphocytes were closely packed and a number of them were in mitotic division. The deep yellow material lining the proximal cavity was composed of granulomatous tissue developing about lipoid. Cholesterol clefts were abundant, and numerous lipoid-laden macrophages were present, together with giant cells. There was no evidence of tuberculous infection. The comment was made that the tissue was an enlarged cervical thymic remnant which had undergone degenerative changes at the

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proximal end. The appearances did not suggest malignancy, but in view of the absence of an enlarged intrathoracic thymus on radiological examination, and in consideration of the rather numerous mitotic figures in the cervical remnant, some suspicion that this might be more than simple hyperplasia seemed justified.

Convalescence was uneventful. On May 1 the child began a course of six deep X-ray treatments to the neck at the Royal Prince Alfred Hospital. He was discharged from hospital on June 9. He had since been examined by Dr. B. E. Frecker at Royal Prince Alfred Hospital, who found no indication for further irradiation. On June 5 an X-ray examination of the chest revealed no abnormality, and a blood count gave normal results.

Angiolipoma of the Right Buttock.

Dr. Steigrad finally showed a baby, aged ten and a half months, who was thought to have an angiolipoma. The baby had had a generalized enlargement of the right leg since birth; the enlargement had grown *pari passu* with the baby.

On examination of the baby, the buttock and leg were enlarged throughout. The enlargement was soft, thick and irregular, with pale reddish nodules. The movements of the joints were normal. There were no other congenital abnormalities. Scattered hæmangiomata were present on the trunk and right buttock. The child was to undergo generalized dissection of the tumour.

Œsophageal Stenosis.

DR. E. H. GOULSTON showed a boy who had suffered from dysphagia from birth; he was usually able to swallow only fluids and took solids only occasionally. At the age of four years his condition was diagnosed as "congenital œsophageal stenosis". Repeated dilatation with bougies brought temporary relief. At the age of seven years a gastrostomy operation was performed by Dr. Hipsley. The child was fed through a tube and orally. A fractional test meal examination revealed complete achlorhydria. At the age of fourteen years he was admitted to the Royal North Shore Hospital with complete obstruction. On December 5, 1951, before operation, a radiological examination was made. The obstruction appeared to be complete; the œsophagus ended in a blind pouch, smooth in contour, and there was considerable dilatation above. Barium was introduced through the gastrostomy and the patient was placed in the Trendelenburg position, when the extent of the occlusion became visible. No hiatus hernia was demonstrated. Œsophago-gastrostomy with excision of the stricture was carried out. Microscopic examination of the tissue removed revealed chronic inflammation; the epithelium was replaced by chronic granulation tissue and hypertrophied muscle. Below the obstruction the tissue was stomach herniated through the diaphragm.

Banti's Syndrome.

Dr. Goulston's second patient was a boy, who had had no neonatal jaundice or sepsis, but had not thriven in his first two months. He had ten siblings alive and well. He had had a hæmatemesis at the ages of nine months, one year, and one year and ten months. On examination of the child in 1944, light brown spots of pigmentation were present on the trunk; neither the liver nor the spleen was palpable. The hæmoglobin value was eight grammes *per centum* and the platelets numbered 200,000 per cubic millimetre. The bleeding time was one-quarter of a minute and the coagulation time four minutes. X-ray examination after a barium meal revealed no abnormality. On September 5, 1944, a further hæmatemesis occurred, and the spleen and liver were palpable. The hæmoglobin value was nine grammes *per centum*, the platelets numbered 250,000 per cubic millimetre, and no abnormal fragility was detected in the erythrocytes. A transfusion of 200 millilitres of blood was given.

On August 31, 1945, a further hæmatemesis occurred and anæmia was present; the spleen was palpable. The hæmoglobin value was 8·6 grammes *per centum* and the platelets numbered 61,800 per cubic millimetre; the leucocytes numbered 4200 per cubic millimetre. X-ray examination of the long bones revealed no abnormality. A transfusion of 360 millilitres of blood was given.

On March 26, 1946, the child had another hæmatemesis; fluctuation in the size of the spleen was observed with the occurrence of hæmatemesis on several occasions in hospital. A transfusion of 400 millilitres of blood was given. Sternal biopsy revealed normoblastic hyperplasia. On May 21, 1946, splenectomy was carried out; examination of the spleen revealed splenic fibrosis consistent with the presence of Banti's syndrome.

On April 15, 1947, the child had hæmatemesis and melæna. His hæmoglobin value was five grammes *per centum* and the plasma protein content was 5·7 grammes *per centum*. A transfusion of 600 millilitres of blood was given. On August 1, 1947, after another hæmatemesis, a transfusion of 1800 millilitres of blood was given. On November 8 there was another hæmatemesis, and a transfusion of 500 millilitres of blood was given.

On July 19, 1948, the child had a further hæmatemesis, and a transfusion of 1400 millilitres of blood was given. No urobilinogen was found in the urine. The prothrombin time was five minutes. The serum bilirubin content was 0·3 milligramme *per centum*; the albumin-globulin ratio was 2·1:1·0.

On March 21, 1949, the child's dental caries was treated. The total serum protein content was 6·8 grammes per 100 millilitres; the albumin-globulin ratio was 2·8. On September 5 the child had a hæmatemesis. The thymol turbidity test result was less than one unit. The thymol flocculation test produced a negative result. X-ray examination with the aid of a barium bolus revealed appearances suggesting the presence of œsophageal varices.

On March 3, 1950, the child had a large hæmatemesis, and was given a transfusion of 1300 millilitres of blood. On April 24 œsophago-gastrectomy was carried out with a thoraco-abdominal approach. Pathological examination of the specimen revealed considerable hæmorrhage into the cardia and some distended and tortuous vessels; none of the vessels were thrombosed. On May 9 the child suffered from an effusion and atelectasis at the base of the left lung; the condition cleared up. On March 16, 1951, he had an effusion and consolidation at the base of the left lung; the condition cleared up under treatment with penicillin. On June 11, 1951, he vomited two or three ounces of bright red blood. He had been well since.

Eventration of the Diaphragm.

Dr. Goulston's last patient was a boy who had been born normally on December 13, 1951; his birth weight was eight pounds. His condition had been normal until two days later, when grunting respiration, lethargy and repeated cyanotic attacks developed. On examination of the baby, heart sounds were heard on the right side of the sternum. X-ray examination revealed a left diaphragmatic hernia containing stomach. The heart was on the right side of the thorax. A fluoroscopic examination on January 8, 1952, revealed no evidence of diaphragmatic hernia or malrotation of the bowel. The left hemidiaphragm was much elevated, but it moved normally. The mediastinum was considerably displaced to the right. The condition was thought to be primarily an eventration on the left side. The symptoms began to subside, and the baby soon compensated for the thoracic lesion. No treatment was instituted, and he was discharged from hospital three weeks later.

(To be continued.)

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

A GOVERNMENT MIDWIFE.[1]

Colonial Secretary's Office,
Sydney,
1 September, 1828.

James BOWMAN, Esq.,
Principal Surgeon.

Sir,

At the recommendation of the Committee of Management of the Female Factory, I am directed to inform you that His Excellency has been pleased to approve of Mary MUMFORD, per HARMONY, now a nurse at the SYDNEY HOSPITAL, being appointed Govt. Midwife in the room of Mary JONES who has tended her resignation.

[1] From the original in the Mitchell Library, Sydney.

The Committee further recommend that, in order to place her more immediately under the control of your Department, and to enable her to attend the poor at their own houses, so as to prevent the necessity of their being received into the Hospital, she may be permitted to reside out of the Establishment, and as she is an elderly woman, this has been sanctioned.

In consideration of her providing herself with a dwelling, food, and clothing, her salary will be the same as that allowed to her predecessor, namely, £20 Twenty Pounds a year.

I have, &c.,

ALEXR. MCLEAY.

Post-Graduate Work.

THE MELBOURNE PERMANENT POST-GRADUATE COMMITTEE.

Course in Surgery.

SUBJECT to a sufficiency of entrants, the Melbourne Permanent Post-Graduate Committee will conduct a course of instruction for higher surgical study, suitable for those entering for the final F.R.A.C.S. examination in May, 1953, commencing on March 16 and finishing on May 1.

The syllabus will comprise 25 clinical demonstrations, which will be held on Mondays, Tuesdays, Wednesdays and Fridays in the afternoon from 3 to 5 p.m. These will be conducted by Mr. G. Brosnan, F.R.C.S., F.R.A.C.S. (Saint Vincent's Hospital), Mr. G. Grove, M.S., F.R.A.C.S. (Alfred Hospital), Mr. I. Heinz, M.S., F.R.A.C.S. (Royal Melbourne Hospital), and Mr. R. Webb, M.S., F.R.C.S., F.R.A.C.S. (Prince Henry's Hospital). Provision will be made for entrants to attend out-patient clinics in the various hospitals. The course will be under the general supervision of Mr. S. F. Reid, M.S., F.R.C.S., F.R.A.C.S.

Those desirous of undertaking this course are asked to communicate with the Secretary of the Melbourne Permanent Post-Graduate Committee at 394 Albert Street, East Melbourne, without delay, as it is essential that the committee learn at an early date the number likely to enter. The fee for the course will be 20 guineas.

SYDNEY INSTITUTE FOR PSYCHO-ANALYSIS.

THE Sydney Institute for Psycho-Analysis will start its second introductory one-year course on psychoanalysis for medical graduates early in 1953. The course will be held fortnightly from 7 p.m. to 9 p.m. on Thursdays at the Council Room of the British Medical Association. Those who wish to participate should apply to the Secretary, Sydney Institute for Psycho-Analysis, Room 3C, Third Floor, 143 Macquarie Street, Sydney.

Australian Medical Board Proceedings.

NEW SOUTH WALES.

THE following have been registered, pursuant to the provisions of the *Medical Practitioners Act*, 1938-1950, as duly qualified medical practitioners: Bridgman, Peter, M.B., B.S., 1950 (Univ. Queensland); O'Brien, Patrick Aloysius, L.R.C.P. (Edinburgh), 1950, L.R.C.S. (Edinburgh), 1950, L.R.F.P.S. (Glasgow), 1950; McElroy, Josephine Bernadette, L.R.C.P. (Edinburgh), 1947, L.R.C.S. (Edinburgh), 1947, L.R.F.P.S. (Glasgow), 1947; Stephen, Bruce Smith, M.B., Ch.B., 1951 (Univ. Aberdeen).

The following additional qualifications have been registered: Bauer, Gaston Egon (M.B., B.S., 1946, Univ. Sydney), M.R.A.C.P., 1952; Gardiner, Leslie Andrew (M.B., B.S., 1936, Univ. Sydney), L.R.C.S. (England),[1] 1952; Kendall, Richard Bruce (M.B., B.S., 1942, Univ. Sydney), D.G.O. (Univ. Sydney), 1952; Scanlan, Frederick Joseph (M.B., B.S., 1944,

[1] There is no such diploma as L.R.C.S. (England). We are informed that F.R.C.S. is meant.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED NOVEMBER 29, 1952.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	1(1)	1(1)	..	..	..	..	..	..	2
Amœbiasis	..	2(2)	1	..	1(1)	..	..	..	4
Ancylostomiasis	..	2(2)	..	..	..	..	..	..	2
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	..	..	..	..	..
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	1	..	..	..	..	..	..	1
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	..	..	29(28)	..	..	..	..	..	29
Diphtheria	4(3)	7(5)	7(2)	2(1)	4(4)	2	..	..	26
Dysentery (Bacillary)	..	4(2)	5(5)	..	1(1)	..	..	..	10
Encephalitis	3(2)	2(2)	..	1	..	..	..	..	6
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	1	..	..	..	..	..	..	1
Infective Hepatitis	..	5(1)	..	..	18(11)	..	..	..	23
Lead Poisoning	..	..	..	..	1	..	..	..	1
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	..	..	..	..	..	..	..
Malaria	..	..	..	..	..	..	..	..	..
Meningococcal Infection	2(2)	12(4)	1	..	1(1)	..	..	..	16
Ophthalmia	..	..	..	..	6	..	..	..	6
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	21(13)	19(11)	4(1)	11(8)	..	17(3)	..	..	72
Puerperal Fever	..	..	..	..	..	..	..	..	..
Rubella	..	177(130)	..	..	3(1)	..	..	..	180
Salmonella Infection	..	..	..	..	..	..	..	..	..
Scarlet Fever	13(8)	35(21)	1	2(2)	2(2)	1	..	..	54
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	..	..	..	..	..	..	..
Trachoma	..	..	..	..	..	..	..	..	..
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	49(37)	16(5)	10(1)	5(4)	2(1)	3(3)	1	1	87
Typhoid Fever	1(1)	..	2(1)	..	..	..	..	..	3
Typhus (Flea-, Mite- and Tick-borne)	..	..	..	..	..	..	..	..	..
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

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Univ. Sydney), D.P.M. (Univ. Sydney), 1952; Storey, Joan Evelyn (M.B., B.S., 1944, Univ. Sydney), M.R.C.O.G., 1952; Stafford, Richard Stanley (M.B., B.S., 1940, Univ. Sydney), M.R.C.O.G., 1952.

QUEENSLAND.

THE following have been registered, pursuant to the provisions of *The Medical Acts*, 1939-1948, as duly qualified medical practitioners: Ivanov, Aksel, M.B., B.S., 1950 (Univ. Sydney); Phibbs, John Douglas, B.M., B.Ch., 1941 (Univ. Oxford); Sandeman, Thomas Fraser, M.B., Ch.B., 1950 (Univ. Edinburgh); Christensen, Frederick George, L.M.S.S., A. (London), 1952; Hopkins, William Allen, M.B., B.Ch., B.A.O., 1936 (Queen's Univ., Belfast), D.L.O., R.C.S. (England), 1951.

The following additional qualifications have been registered: Petherbridge, Clyde Tyrer, D.D.M. (Univ. Sydney), 1952; Marks, James Keith Livingstone, D.G.O. (Univ. Sydney), 1952.

Notice.

A WARNING.

READERS are warned against a young woman who has been visiting consultants, saying that she has been recommended by a Lithgow doctor, and who has been obtaining money by saying that she has lost her purse and her return ticket to Lithgow.

Nominations and Elections.

THE undermentioned has applied for election as a member of the New South Wales Branch of the British Medical Association:

Cotton, Keith Lucas, M.B., B.S., 1952 (Univ. Sydney), 6 Lisgar Road, Hornsby, New South Wales.

The undermentioned have applied for election as members of the South Australian Branch of the British Medical Association:

Pryor, William John, M.B., B.S., 1952 (Univ. Adelaide), 19 Ralph Avenue, West Croydon, South Australia.

Dunn, John Edgar, M.B., B.S., 1952 (Univ. Adelaide), 38 East Terrace, Kensington Gardens, South Australia.

Waterhouse, Ronald Greaves, M.B., B.S., 1952 (Univ. Adelaide), 29 Marlborough Street, College Park, South Australia.

McCartney, James Elvins, M.B., Ch.B., M.D., D.Sc. (Univ. Edinburgh), 1915, 16 Sherbourne Road, Medindie Gardens, South Australia.

Quinn-Young, Michael, M.B., B.S., 1952 (Univ. Adelaide) (qualified 1951), 77 The Grove, Lower Mitcham, South Australia.

The undermentioned have been elected as members of the South Australian Branch of the British Medical Association: Heitmann, John Smith, M.B., B.S., 1951 (Univ. Adelaide) (qualified 1950); Mutze, George Friedrich, M.B., B.S., 1952 (Univ. Adelaide) (qualified 1951).

The undermentioned have been elected as members of the New South Wales Branch of the British Medical Association: Brown, Bruce Alexander, M.B., B.S., 1952 (Univ. Sydney); Connolly, John Anthony, M.B., B.S., 1952 (Univ. Sydney); Keatinge, Richard Harte, M.B., B.S., 1952 (Univ. Sydney); Morgan, Michael Francis, M.B., B.S., 1952 (Univ. Sydney); Muir, William McCartney, M.B., B.S., 1952 (Univ. Sydney); McFadden, John Brian, M.B., B.S., 1951 (Univ. Sydney); Morris, Marion Erica, M.B., B.S., 1950 (Univ. Sydney); Mulhearn, Michael Harry Gerald, M.B., B.S., 1941 (Univ. Sydney); Berents, Helen, M.R.C.S. (England), L.R.C.P. (London), 1940.

Medical Appointments.

Dr. Maureen Grattan-Smith has been appointed to the Department of Public Health of New South Wales.

Dr. Clara Campbell and Dr. J. L. Evans have been appointed to the Division of Mental Hygiene, Department of Public Health, of New South Wales.

Dr. A. Millar has been appointed a member of the Physiotherapists' Registration Board of Tasmania.

Dr. H. E. Pellew has been appointed honorary gynæcologist at the Royal Adelaide Hospital.

Dr. A. D. Byrne has been appointed honorary assistant gynæcologist at the Royal Adelaide Hospital.

Dr. R. M. C. G. Beard has been appointed honorary clinical assistant to the gynæcological section of the Royal Adelaide Hospital.

Diary for the Month.

JAN. 6.—New South Wales Branch, B.M.A.: Council Quarterly.
JAN. 7.—Western Australian Branch, B.M.A.: Council Meeting.
JAN. 8.—South Australian Branch, B.M.A.: Council Meeting.
JAN. 13.—New South Wales Branch, B.M.A.: Executive and Finance Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

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